



ZOONOTIC INFLUENZA

Detection, Response, Prevention, and Control Reference Guide



nasphv

national association of state
public health veterinarians



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TERRITORIAL EPIDEMIOLOGISTS

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Background

This reference guide was produced as a collaborative project between the U.S. Centers for Disease Control and Prevention (CDC), the National Association of State Public Health Veterinarians (NASPHV), and the Council of State and Territorial Epidemiologists (CSTE). Primary informants and contributors to the project are listed below. Report content was prepared by Meghan Schaeffer, EdD, MPH, MPA. The project’s primary sponsors were James Kile, DVM, MPH, DACVPM, CPH of CDC and Ashley Vineyard of CSTE. The CSTE Zoonotic Influenza Workgroup provided regular feedback in workgroup meetings and with general project support. Other subject matter experts from the National Association of State Animal Health Officials (NASAHO) contributed as needed.

Key Contributors

Name	Title	Agency
Dr. James Kile	Health Scientist	CDC/Influenza Division
Dr. Maggie Baldwin	Colorado State Veterinarian	Colorado Department of Public Health
Dr. Kelly Geisbrecht	State Public Health Veterinarian	Kentucky Department of Public Health
Dr. Amber Singh	State Public Health Veterinarian	(formerly) Ohio Department of Public Health
Dr. Brandy Darby	Veterinarian Epidemiologist	Virginia Department of Health

Purpose Statement

The purpose of this document is to serve as a repository for up-to-date information on animal and zoonotic influenza, addressing major events of interest, lesser-known viruses with the potential for future impact, and isolated events with any probability of human impact. The guide is also focused on surveillance, epidemiology, prevention, and control of events of animal outbreaks or novel human infections with animal and zoonotic influenza viruses. The guide is intended to support state and local animal and public health officials in acquiring rapid situational awareness of an animal or zoonotic influenza event, including novel human infections, though it also provides a broad background and historical information on influenza in humans and animals. With the ever-changing landscape of influenza viruses, their presence and emergence in various species, and improved surveillance and epidemiology over time, a comprehensive resource is needed to support the future of animal and human health control and prevention efforts.

How to Use This Guide

This reference guide was created to provide state and local animal and public health officials with an accessible, easy-to-use resource for understanding and managing novel and emerging situations involving animal and zoonotic influenza viruses. The content was obtained through an extensive textbook, journal article, and web source review along with subject matter interviews with veterinarians, epidemiologists, and other animal health and public health professionals.

The guide is organized by both animal species and influenza virus subtypes to facilitate search by either, depending on the situation. General information about all known influenza virus strains is included as background for potential situations, whether zoonotic transmission resulting in human illness or suspected infection or where a zoonotic event simply occurred. Where possible, direct links to resources are provided. All citations are hyperlinked to their position in the bibliography (ctrl+click).

Influenza Viruses Background

Influenza viruses belong to the family *Orthomyxoviridae* and are differentiated into 4 types: influenza A, influenza B, influenza C, and influenza D. *Isavirus*, *Thogotovirus*, and *Quaranjavirus* are also part of the *Orthomyxoviridae* family, though they are of little consequence to humans.^{8,9} IAVs are significant pathogens of humans and animals. All influenza A and B viruses contain 8 genomic sequences coding for 11 proteins, including:⁸

- Hemagglutinin (HA)
- Neuraminidase (NA)
- Nucleoprotein (NP)
- Matrix (M1) protein
- Matrix (M2) ion channel
- Two “polymerase basic” (PB1, PB2) subunits
- Polymerase acidic (PA) subunits
- Accessory protein (PB1-F2)
- Nonstructural protein (NS1)
- Nuclear export protein, also referred to as nonstructural protein 2 (NS2)

Influenza C and D have 7 gene segments, with the hemagglutinin-esterase-fusion (HEF) gene replacing the HA and NA surface proteins found in A and B strains.^{6,10-12} Influenza viruses have single-stranded ribonucleic acid (RNA) negative-sense genomes.^{12,13}

Influenza A Viruses

Influenza A viruses (IAV) are known to widely circulate in humans, wild birds, domestic birds, swine, equine, canines, and bats, with the potential to cause seasonal and sporadic epidemics in humans and swine.¹⁴⁻²⁴ Occasional infections have occurred in marine animals, ostriches, pandas, and other animals. IAV are differentiated into subtypes based on their surface proteins.^{14,15,22,23} Within the genera of IAV, subtypes for HA and NA extend to 18 subtypes for HA and 11 for NA.⁸ The HA structural proteins are responsible for cellular receptor binding and membrane fusion and can function with a significant amount of genetic change. The NA proteins support the release of the virion from the host cell and help the virus break through the mucous membrane of the respiratory tract to infect host cells.^{8,9,25,26}

More than 130 IAV subtypes have been identified in nature, mostly in avian species.⁶ With the exception of H17, H18, N10, and N11, all probable combinations have been found in birds. Additionally, almost all IAV subtypes were originally isolated from avian hosts, though not the 2 known bat IAVs (Figure 1).^{6,9}

HA-Subtype	NA-Subtype	Human	Swine	Equine	Domestic Poultry	Waterfowl Shorebirds	Sea Mammals (Seal/Whale)	Bat
H1	N1	H1/N1	H1/N1		H1/N1	H1/N1	H1	
H2	N2	H2/N2	H2/N2		H2/N2	H2/N2	N2	
H3	N3	H3/N3	H3	H3	H3/N3	H3/N3	H3/N3	
H4	N4	N4	H4		H4/N4	H4/N4	H4	
H5	N5	H5	H5		H5/N5	H5/N5	N5	
H6	N6	H6/N6	H6/N6		H6/N6	H6/N6		
H7	N7	H7/N7		H7/N7	H7/N7	H7/N7	H7/N7	
H8	N8	N8		N8	H8/N8	H8/N8		
H9	H9	H9/H9	H9		H9/N9	H9/N9	N9	
H10	N10	H10			H10	H10	H10	N10
H11	N11				H11	H11		N11
H12					H12	H12		
H13					H13	H13	H13	
H14					H14	H14		
H15					H15	H15		
H16					H16	H16		
H17								H17
H18								H18

Figure 1. Reports of influenza A virus hemagglutinin (HA) and neuraminidase (NA) subtypes by species. Mostafa, et al, 2018⁶

Wild aquatic birds are the natural reservoirs of IAVs. While IAVs have been isolated from over 100 species of birds, ducks or mallards are the most common source, followed by gulls and shorebirds.²⁷ In aquatic birds, influenza replicates primarily in the intestinal tract, spreading in water via fecal-oral mechanisms. The congregation of birds at breeding and overwintering grounds also provides opportunities for transmission and reassortment of IAVs.¹³ Interestingly, influenza viruses in these bird reservoirs show limited evolution. It is only when these viruses spread to other hosts that rapid changes occur, resulting in antigenic variants.²⁸

Human IAVs have only acquired new genetic segments from avian or other sources in the 4 major pandemic events in the last 100 years.²⁹ Outside of the occurrence of a pandemic, the primary construct of the IAV in humans evidenced drifting changes to its genome. While interspecies or zoonotic transmission occurs frequently between swine and humans, birds or humans are often the source of a novel infection in swine with IAV.³⁰

Influenza A is also endemic in swine populations. Influenza was first detected in swine in 1930 following the 1918 pandemic and was confirmed as A(H1N1).³¹ Swine have been the source of sporadic human infections with swine influenza viruses and were not considered a pandemic threat until an outbreak occurred among military recruits in 1976.³² The ability of the virus to quickly infect several hundred recruits with an assumed person-to-person spread was initially alarming. However, the outbreak did not become a pandemic. In 1998, a substantial reassortment event introduced new endemic swine strains that set the stage for the 2009 A(H1N1)pdm09 pandemic.³³⁻³⁵

Influenza B Viruses

Influenza B viruses (IBV) are isolated almost exclusively from humans. Infection has also been detected in seals, which may serve as a reservoir.^{23,36} Like influenza A, IBV have 8 discrete gene segments, each coding for at least 1 protein.⁶

IBV are defined by lineage, not surface proteins. There are 2 lineages—B/Yamagata and B/Victoria—both of which emerged as antigenic variants in the 1970s and have cocirculated since 2001.⁹ The HA gene of IBV evolves at a much slower rate compared to the HA genes of IAV. For reasons not well understood, both lineages have caused high levels of epidemic activity, disproportionately affecting young children and the elderly. Future circulation of the B/Yamagata lineage may change as the 2019 SARS-CoV-2 pandemic may be pushing the virus to extinction as it has been detected only minimally since April 2019.^{9,31,37}

Influenza C Viruses

Influenza C viruses cause cold-like symptoms in humans and occasionally lower respiratory infection in children younger than 2 years of age. IAV infections cause mild illness in humans and are not known to cause epidemics.⁹ Like influenza B, influenza C is found primarily in humans, though it can also be found in dogs, cattle, and swine.^{32,36,38,39} Serologic studies show evidence of prior infection in up to 90% of children aged 7 to 10 years, suggesting widespread exposure to IAV in human populations.⁴⁰

Influenza C viruses have only 7 gene segments and a single surface glycoprotein that acts as HA and NA functionally in one called the HEF protein.⁸

Influenza D Viruses

Influenza D viruses (IDV) affect cattle, other ruminants, and swine. They are not known to cause disease in or infect people despite serologic evidence in cattle workers.^{9,41-44} Discovered in 2011 in swine in Oklahoma, IDV have subsequently been detected in multiple animal species.³² Bovids are considered the major reservoir for IDV, which

may play a role in bovine respiratory disease. Seroprevalence survey shows up to 77% positivity with the highest rates in the upper Midwest and Mountain West.^{41,45} The zoonotic potential of influenza D is controversial as cattle workers have demonstrated serologic evidence of influenza D infection. It is unknown whether influenza D causes disease in humans.⁴⁴

Similar to influenza C, IDV have the HEF protein equivalent to HA and NA glycoproteins. There are 2 lineages of influenza D: D/OK (location of initial identification) and D/Japan.⁴¹

Influenza A Naming Conventions

For more than 40 years, influenza virus naming conventions have followed an internationally accepted standard.^{4,46} Each IAV name contains the antigenic type (A), the host species of origin (e.g., swine, equine) if the original host is nonhuman, geographical origin (e.g., California, Tokyo), strain number (not related to the HA or NA subtype), and year of collection.^{9,46,47} The HA and NA description is provided in parentheses at the end of the virus name. To distinguish the A(H1N1) pandemic virus from the seasonal A(H1N1) strain circulating before the 2009 pandemic, the virus was named A(H1N1)pdm09.⁴⁷ One further unique feature of influenza naming conventions is a "v" (variant), which is added when an influenza virus that usually circulates in swine is detected in human infection (e.g., A(H3N2)v).⁹

Genetic Sequencing of Influenza Viruses

Genomic sequencing, the process of determining the order of nucleotides (i.e., A, C, G, U) in influenza viral RNA, is performed on approximately 7,000 specimens per year by CDC and National Influenza Reference Centers.^{4,48}

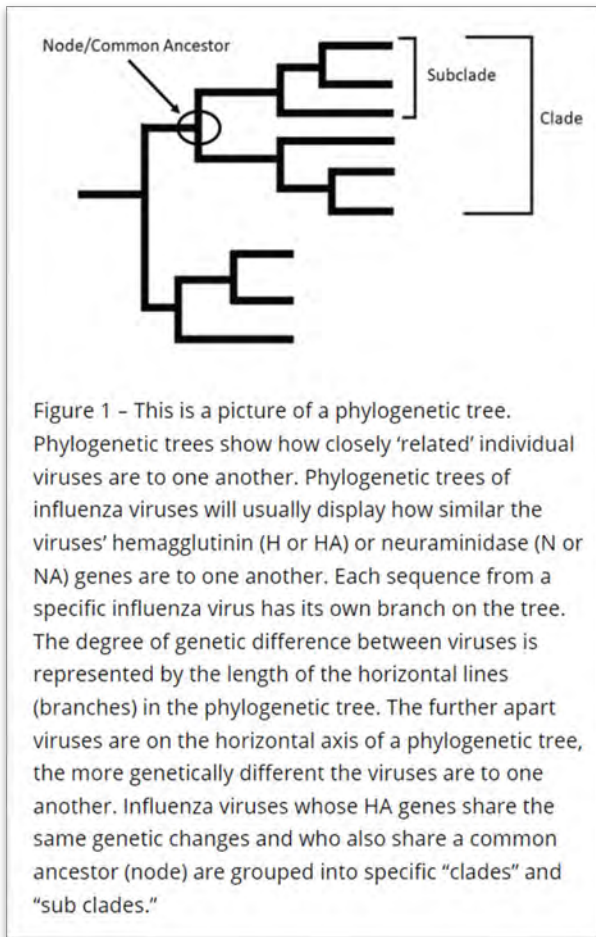


Figure 2. Phylogenetic tree example. CDC, *Types of Influenza Viruses, 2021*⁴

When looking at the genomic characterization of influenza virus types A and B, influenza A further splits into subtypes while influenza B is parsed into lineages only. Subtyping of IAV continues into lineages under which viruses are differentiated by clades, then subclades, also referred to as groups and subgroups (Figure 2). Clades are organized by similarities in their HA gene sequences, though phylogenetic trees may be created for any influenza gene. Within genetic sequencing or phylogenetic trees, clades and subclades are tied to a "single common ancestor" displaying further genetic changes within a node or grouping (Figure 2).⁴ The degree of genetic difference between viral sequences is represented by the length of horizontal lines in the phylogenetic tree, with shorter lines representing greater genetic similarities. This approach to the detailed characterization of influenza types is in response to the extensive genetic evolution and reassortant ability of IAV.^{4,50}

Additional information on genetic sequencing may be found here: [Influenza Virus Genome Sequencing and Genetic Characterization](#)

Antigenic Drift and Shift

Two phenomena of genetic change are commonly discussed in the influenza virus literature: antigenic drift and antigenic shift. Antigenic drift occurs with subtle changes in the genetic composition of a virus over time (usually accumulated through replication errors).^{4,9} Although natural selection perpetuates versions of the virus more fit than the last, the result does not typically affect how the virus impacts its host. The culprit in making replication errors is polymerase, or the proofreading function in viral RNA replication.^{50,51} While antigenic drift occurs in all species that are commonly and routinely infected with influenza viruses, human strains have more point source mutations than any other species.⁵²

Replication errors occur relatively more frequently in RNA viruses compared to DNA viruses, because the viral RNA polymerase enzyme, responsible for synthesizing genetic copies of the viral genome, is notorious for allowing errors to occur during the replication process, which results in the replicated genome varying from the “parent” genetic material being copied.^{50,51} Once these replication errors occur, the RNA polymerase is unable to correct them, which is why this enzyme is sometimes said to have a poor proofreading ability. Although natural selection perpetuates versions of the virus more fit than the last, changes that arise through antigenic drift do not typically result in significant changes to the functionality of the virus.^{50,51}

Antigenic shift is less common than antigenic drift, and viruses resulting from antigenic shift can pose substantial threats to human and animal health. Antigenic shifting happens through the interspecies transfer of the whole virus to a new host species (animal or human) or considerable genetic reassortment.⁸ With interspecies transfer, a virus has developed or can adapt or acquire a receptor affinity that enables it to more easily infect a new species. Reassortment typically results from infection of a single animal or human host with 2 or more different influenza viruses, in which parts of each virus are selected into a newly replicated one.⁵¹ Even with extensive study of animal reservoirs, it is extremely difficult to predetermine the antigenicity and virulence of a reassorted virus.

Influenza in Humans

Burden of Disease, Clinical Symptoms, Transmission, and Risk Factors

Human influenza is a major respiratory disease, causing illness in 1 billion people globally every year, with approximately 290,000-650,000 deaths.^{49,53} In the United States, the Centers for Disease Control and Prevention (CDC) estimates between 9 and 41 million illnesses, 140,000-710,000 hospitalizations, and 12,000-52,000 deaths annually.^{54,55} An average of 8% of the US population (range, 3% to 11%) experiences influenza illness every year.⁵⁶ Influenza A and B strains circulate seasonally, with A typically causing more severe illness. In temperate countries, the virus circulates in the winter months, while tropical and subtropical countries experience year-round infections, though at a lower rate than that in temperate countries. Influenza follows a hemispheric and seasonal pattern in which fall and winter seasons during the months of June-August in the Southern Hemisphere align with increased influenza activity, while in the Northern Hemisphere, December-March are the dominant months for influenza activity.^{50,57}

Influenza causes rapid onset of fever, fatigue, cough, sore throat, headache, body aches, conjunctivitis, and, in severe cases, pneumonia. Acute symptoms, including fever, can last for 7 to 10 days, though fatigue and weakness may last for longer.^{51,58} Flu spreads from person to person through aerosolized droplets containing the influenza virus. Droplets are expelled from infected people when coughing, sneezing, or talking and may be inhaled through the nose or mouth of an uninfected person. Less often, influenza is spread after contact with a contaminated surface when a person touches their mouth, nose, or eyes.⁵⁸

Symptom onset is approximately 2 days following exposure, with an incubation period ranging from 1 to 4 days. An infected person may be contagious up to 1 day before symptoms appear through 5 to 7 days after illness onset. Infected people are most contagious 3 to 4 days after the onset of symptoms. Immunocompromised, older, and younger people may be contagious for longer than 5 to 7 days.⁵⁶

Persons 65 years and older, those with certain chronic health conditions, pregnant people, and children younger than 5 years are at increased risk for developing influenza-related complications such as pneumonia, myocarditis, encephalitis, myositis, rhabdomyolysis, and multiorgan failure.^{59,60}

Prevention and Treatment

Vaccination is the most effective way to prevent influenza. The vaccine can result in milder influenza illness, shorter duration, and a reduced risk for hospitalization and death. As of 2021, the influenza vaccine in the United States protects against 4 flu

viruses: 2 influenza A strains (typically one strain of A(H3N2) and A(H1N1)pdm09 and 2 influenza B strains (B/Victoria and B/Yamagata).^{58,61,62} Everyone 6 months and older is advised to get an annual flu vaccine, preferably by the end of October.^{58,61}

Four antiviral medications are available and recommended for the treatment of influenza: oseltamivir, zanamivir, peramivir, and baloxavir. Oseltamivir and baloxavir are taken orally, zanamivir is inhaled, and peramivir is administered intravenously. Antivirals may reduce complications associated with influenza infection.⁶³ Antiviral treatment works best if administered shortly after the onset of illness.

For detailed information regarding seasonal influenza vaccination in humans, refer to the [Human Vaccines](#) section.

Dominant Influenza Subtypes in Humans

Human immunogenicity to seasonal influenza over the past 100 years generally involves hemagglutinin (HA) subtypes H1, H2, and H3.⁶⁴ As pandemic events occurred over the last century, each had an impact on which strains circulated seasonally in the post-pandemic period, as evidenced by the continuous presence of A(H1N1)pdm09 in recent influenza seasons. While occasional interspecies transmission occurs, most often from domestic poultry to humans or between swine and humans, person-to-person transmission is not typical after the initial interspecies transmission event.^{65,66}

Humans are immunologically naïve to A(H5) and A(H7) subtypes, which is why these avian influenza virus subtypes are of significant concern. If either strain acquired the ability to spread easily from person to person, a global pandemic could ensue.⁶⁷

Human Pandemics of the Last 120 Years

The following section details major pandemics since 1900 as designated by the World Health Organization (WHO). According to the WHO, a pandemic is an “epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a very large number of people.”⁶⁸ For context, “epidemic” refers to an increase, usually sudden, in the number of cases of a disease that exceeds what is expected in a population. Epidemics are usually preceded by and outbreak, which is an epidemic in a more limited geographic area.⁶⁹

The impact of historical pandemics was typically measured in terms of excess mortality and extrapolated burden of disease per population. Data for the 1918-1919 pandemic was tracked for approximately three-quarters of US states and territories.⁷⁰ Virus identification was available after 1932, and it was after this time that patterns in how pandemics affected seasonal influenza were established.⁷⁰ Each major pandemic and

one epidemic changed the influenza strains that circulated, a pattern that continues today.⁷⁰⁻⁷⁴

Two epidemics were included in the following listing because one in 1976 resulted in a significant public health response in the United States, and a second in 1977 altered the circulation of seasonal influenza by adding an A(H1N1) virus.^{5,75,76}

TABLE 1. Excess deaths estimated for pandemic and interpandemic periods, 1918–1991

Period	Years	No. of excess deaths	Annual average	Crude rate per 100,000 persons
<i>Pandemic</i>	1918–1920	675,000	225,000	218.4
<i>Interpandemic</i>	1920–1933	368,400	28,338	23.0
<i>Interpandemic</i>	1933–1957	242,600	10,108	7.5
<i>Pandemic</i>	1957–1960	115,700	38,567	22.0
<i>Interpandemic</i>	1960–1968	114,900	14,363	7.5
<i>Pandemic</i>	1968–1972	111,927	27,982	13.9
<i>Interpandemic</i>	1972–1981	198,800	22,089	10.3
<i>Interpandemic*</i>	1981–1991	200,000†	20,000	10.0

• Preliminary estimates.
† Approximation.

Figure 3. Crude death rates for pandemic and interpandemic periods, 1918-1991, Kilbourne, et al., 2006⁵

1918/1919–H1N1 (Spanish Flu)

This pandemic is marked as the most significant in the recorded history of influenza, killing an estimated 40 to 50 million people.^{74,77} Its exact origin is unknown, although some believe it may have started in the United States. Sporadic illness occurred in the United States in the spring and early summer of 1918, likely seeding around the world with the movement of troops fighting in World War I.^{70,78} The first major wave took place in October with a second in late winter. The A(H1N1) pandemic was unusual in that it affected those aged 20 to 40 years most severely; persons older than 65 years accounted for less than 1% of excess deaths in 1918 (Figure 3).⁵

There are mixed theories as to the origin of the A(H1N1) pandemic virus. The internal genome of the A(H1N1) pandemic IAV may have originated from an equine H7N7 strain sometime in the late 1800s, with subsequent reassortment to acquire a human A(H1) subtype and an avian N1.^{5,52,79} The pandemic A(H1N1) virus continued to circulate widely for several decades until 1957, causing a few severe epidemics.

1957–H2N2 (Asian Flu)

First identified in East Asia in 1957, this A(H2N2) strain was composed of 3 different avian influenza genes including those for hemagglutinin and neuraminidase.⁷¹ This strain demonstrated similar patterning to the A(H1N1) Spanish flu, with a late October wave and a second peak in February. Total excess mortality, although substantial in exceeding 1 million, was one-tenth that of the Spanish flu pandemic.⁷⁰ This virus

continued to circulate for 10 years after the pandemic, producing one major epidemic before the next pandemic in 1968.⁷⁰ With the arrival of this strain, A(H1N1) disappeared from human infections until 1977.⁸⁰

1968–H3N2 (Hong Kong Flu)

H3N2 arose from the genetic reassortment of low pathogenicity avian influenza (LPAI) viruses and human influenza A viruses (IAVs). One of the 2 avian-origin genes contained in this virus was a new A(H3) hemagglutinin; the N2 was from the 1957 Asian flu virus.^{5,72} The virus circulated in the United States as early as September 1968 but did not surge until December. This pandemic affected persons older than 65 years most severely and caused approximately 1 million total deaths.^{70,72} This is 1 of the 2 human seasonal IAVs still circulating today.

1976–Fort Dix (the pandemic that was not)–Notable Outbreak

A novel A(H1N1) virus was detected in 230 military recruits, resulting in 1 death. In anticipation of the potential for a widespread epidemic, 40 million people were vaccinated, resulting in 532 cases of Guillain-Barre syndrome and 32 deaths.⁸¹ The transmissibility of this virus was substantially lower than that of *influenza* viruses in previous pandemics, and because of the “tight social-contact structure of the military training base,” transmission was not sufficient to reach epidemic proportions.^{80,82}

1977–H1N1 (Russian Flu)–Notable Epidemic

Russian flu, a reemergent A(H1N1) strain, caused severe human infections in those younger than 26 years and a 50% fatality rate among children.^{24,83,84} Case rates were estimated at < 5 per 100,000, which was far less than any preceding pandemic or interpandemic event.⁸⁵ In 1977, individuals younger than 26 years had not been exposed to an A(H1N1) strain, as its last wide circulation was before 1957.⁸⁵ Studies showed this strain was closely related to a 1950 strain, yet dissimilar to the 1947 and 1957 strains, and had retained genetic integrity since 1950.^{5,76} The strain is believed to have leaked from a laboratory.^{28,86,87} Cases were first noted in the Soviet Union followed by the United States and other countries. It was after this epidemic that this strain of A(H1N1) began seasonal cocirculation with A(H3N2), the first time 2 influenza A serotypes circulated at the same time.⁸⁸

2009–H1N1

A unique genomic constellation derived from North American avian, Eurasian avian-like swine, A(H1N1) classical type swine influenza, and human seasonal A(H3N2) influenza viruses resulted in the A(H1N1)pdm09 virus.^{35,80,85} First reported in April 2009, the pandemic reached 208 countries with 13,554 deaths in the United States

and up to 575,000 deaths worldwide. The (H1N1)pdm09 strain remains a dominant seasonal influenza virus strain today.⁷³

Zoonotic Influenza Nomenclature

Zoonotic transmission of influenza viruses can occur, both from animals to people and from people to animals, usually through direct contact with an infected host. Most animal influenza viruses are restricted in their ability to infect humans; however, the frequency of zoonotic transmission is increasing (Figure 4).^{7,89}

The nomenclature used to describe specific incidents of human infection with animal-origin influenza viruses in the literature and across international surveillance agencies deviates slightly from the aforementioned definitions. In reports published by CDC,

Subtype Group	Year First Detected	Year Last Detected	Countries ^a of Occurrence	Confirmed Cases, No.; Confirmed Fatalities, No.	Representative Reference(s) for Each Country
H1N1v	1958	2016	Canada, China, Czechoslovakia, Italy, Netherlands, Russia, Spain, Switzerland, Thailand, US	41; 6	[3, 9–16]
HPAI H7N7	1959	2003	Australia, US, Netherlands	91; 1	[7, 17, 18]
LPAI H7N7	1979	2013	US, Italy, United Kingdom	5; 0	[6, 19, 20]
H3N2v	1992	2017	Canada, Hong Kong SAR, Netherlands, US, Vietnam	380; 2	[14, 21–24]
HPAI H5N1	1997	2017	Azerbaijan, Bangladesh, Cambodia, Canada, ^b China, Djibouti, Egypt, Hong Kong, Indonesia, Iraq, Laos, Myanmar, Nigeria, Pakistan, Thailand, Turkey, Vietnam	856; 453	[25–27]
LPAI H9N2	1998	2015	Bangladesh, China, Egypt, Hong Kong, SAR ^b	36; 1	[28–31]
LPAI H7N2	2003	2017	United Kingdom, US	7; 0	[8, 32, 33]
HPAI H7N3	2004	2012	Canada, Mexico	4; 0	[34, 35]
LPAI H10N7	2004	2012	Australia, Egypt	4; 0	[36, 37]
LPAI H7N3	2006	2006	United Kingdom	1; 1	[18]
H1N2v	2007	2015	Brazil, Philippines, US	10; 0	[14, 16, 38]
LPAI H7N9	2013	2017	Canada, ^b China, Malaysia, ^b Taiwan ^b	1393; 534	[39]
LPAI H10N8	2013	2014	China	3; 2	[40]
LPAI H6N1	2013	2013	Taiwan	1; 0	[41]
HPAI H5N6	2014	2016	China	17; 12	[42]
HPAI H7N9	2017	2017	China, Taiwan ^b	8; 4	[43]

Adapted and updated from articles by Perdue and Swayne [25], Myers et al [44], and Freidl et al [45]. Influenza viruses that normally circulate in swine are called “variant” viruses and are designated by the letter v (eg, “H1N1v”) when they occur in humans. Human infections with novel influenza viruses, including variant influenza viruses, were notifiable diseases only after the revision of the International Health Regulations in 2005.

Abbreviations: LPAI, low-pathogenicity avian influenza virus; HPAI, high-pathogenicity avian influenza virus; SAR, Special Administrative Region of China.

^aIncludes Taiwan and Hong Kong SAR.

^bImported case(s).

Figure 4. Zoonotic influenza A virus (IAV) infections in humans. Widdowson, et al, 2017⁷

“novel” influenza A infections include swine and avian, until recently only swine-to-human transmissions had been reported in the United States.¹² The WHO reports differentiate infection by species as “Avian Influenza Viruses” and “Swine Influenza Viruses.”⁶⁹ The use of “novel” or “variant” influenza infection in humans in literature frequently refers to swine-to-human transmission.

Per the CDC definition, novel influenza viruses that usually circulate among animals have been recently identified as having the ability to infect humans and are genetically distinct from human seasonal influenza viruses.¹²

Novel IAV infections in humans are of particular interest as they have significant potential to spread from person to person. The impact of these viruses depends on the species subtype. Avian human infections range from asymptomatic to severe, while swine virus infections are typically asymptomatic to mild.⁸⁴ Events of human infection with avian or swine influenza viruses are closely monitored because of their newly emergent nature and potential threat to human health.

Increasing Incidence of Zoonotic Influenza A Viruses in Humans

In the past 30 years 3 major events have contributed to the significant concern for a potentially severe influenza pandemic: (1) the emergence of a triple reassortant A(H1N1) pandemic virus in humans from swine, (2) the endemic presence of LPAI viruses in birds, and (3) increasing distribution of highly pathogenic avian influenza (HPAI) viruses in birds.⁷ Low pathogenicity avian influenza (LPAI) A(H9N2) viruses are endemic in domestic poultry, primarily throughout Asia, the Middle East, and Africa.²⁴ They frequently cocirculate with A(H5) and A(H7) viruses and have caused an increasing number of human infections since 2015. This virus has also contributed internal influenza viral genes to other avian strains. HPAI A(H5) viruses have spread throughout most of the world, and while currently maladapted for efficient person-to-person transmission, the potential to reassort and gain that function is possible.⁹⁰ A(H5) avian infection in humans can range from asymptomatic to severe, and while human infections of A(H5) have tapered off globally in recent years a greater diversity of avian influenza strains is infecting humans. In the U.S., HPAI A(H5) viruses did not affect domestic poultry until 2014, activity tapered the following year, and now are increasingly present in wild birds with rampant outbreaks once again in poultry.⁹¹

Improvements in surveillance and reporting conducted by the WHO Global Influenza Surveillance and Response System have increased the quantity and diversity of viral strains detected in 123 countries.⁹² The WHO is increasingly focusing on surveillance, aggregation, and reporting of human health events of interest and importance given that it is the only entity able to extract case reports from the majority of countries.⁹² In addition, the World Organisation for Animal Health (OIE) strives to outline standards for animal health management, quarantine, disease prevention, surveillance, and vaccine recommendations.⁹³ CDC One Health is the head of the OIE Collaborating Centre for Emerging and Re-emerging Zoonotic Diseases and a CDC liaison to the Food and Agriculture Organization of the United Nations (FAO). One Health is responsible for coordinating partners in human, animal, and environmental health,

providing subject matter expertise, and developing tools and training materials to prevent, detect, and respond to zoonotic disease events.^{94,95}

The effectiveness of animal and human surveillance systems depends on the ability to detect and respond to incidents as close as possible to the origin and onset of each event.⁹⁶ Interspecies transmissions of highly pathogenic or reassorted avian or swine influenza viruses have resulted in an enormous mass culling of animals, damaging economies and individual livelihoods, as well as jeopardizing human health, whether with isolated cases or on a larger scale, as happened with the 2009 A(H1N1) pandemic.⁹⁶⁻⁹⁹ These events have served as motivating factors to support local surveillance efforts. More information on animal and human influenza virus surveillance and zoonotic infections in humans is located in a later section of this reference guide [Influenza Detection and Response](#).

Surveillance data summaries of novel IAVs in the United States are published here: [Novel Influenza A Virus Infections \(cdc.gov\)](#). This site provides cases by state, season, and subtype, as well as by case characteristics.

Avian Influenza Viruses of Concern

Avian influenza viruses (AIVs) do not circulate in humans, though they can be transmitted to humans and can cause mild to severe illness, including death. Most instances of zoonotic human infection with AIV resulted from direct or proximal contact with infected poultry. Subtypes of AIV known to infect humans include H5, H6, H7, H9, and H10.⁶⁶

Swine Influenza Viruses of Concern

Classifications of zoonotic human infections with swine influenza viruses (SIVs) circulating among swine are slightly different from human influenza naming conventions. When these instances occur, a letter "v" for variant is added to the SIV subtype name (e.g., A(H1N1)v, A(H3N2)v, A(H1N2)v).^{66,100} It is important to note that the occurrence of a swine influenza virus infection in a human may be an isolated event; it does not typically involve a new or variant virus. The term *novel* is widely applied to events of human infections with animal influenza viruses.⁸⁴ To differentiate human infections with swine influenza virus from animal infections with swine influenza virus, the term *variant* is sometimes used. Most human infections with SIV are mild, with much less severe illness and mortality compared to infection with AIV. Known variant strains in the United States resulting in human infection include A(H1N1)v, A(H3N2)v, and A(H1N2)v.^{67,101}

Identification of Situations of Interest–International Situations–Tool for Pandemic Risk Assessment and Influenza Risk Assessment Tool (CDC)

Domestic Situations

The CDC Influenza Risk Assessment Tool (IRAT) is used to evaluate the risk posed by animal influenza viruses with the potential to spread to humans. The tool assesses pandemic potential based on “emergence” and “public health impact” factors. The IRAT is managed by CDC, but most of the viruses assessed have been animal influenza viruses detected internationally and assessed by subject matter experts in other countries.⁷⁰ The IRAT criteria were reviewed and updated in 2018.¹⁰²

According to CDC,¹⁰²

“Emergence” refers to the risk of a novel (i.e., new in humans) influenza virus acquiring the ability to spread easily and efficiently in people. “Public health impact” refers to the potential severity of human disease caused by the virus (e.g., deaths and hospitalizations) as well as the burden on society (e.g., missed workdays, the strain on hospital capacity and resources, and interruption of basic public services) if a novel influenza virus were to begin spreading efficiently and sustainably among people.

Ten risk elements are used to quantify the pandemic potential for an influenza strain. Element scores are weighted based on their significance in either “emergence” or public health impact.” The 10 risk elements are defined by CDC as follows:¹⁰²

Properties of the Virus category contains 4 of the 10 risk elements, including:

***Genomic analysis** is a measure of the extent of genetic diversity or the presence of known molecular signatures important for human infections and disease.*

***Receptor binding** refers to the host preference (e.g., animal or human) of an influenza virus as well as the types of tissues and cells the virus is best suited to infecting (e.g., nose tissue and cells vs. deep lung tissue and cells). Some influenza viruses are better adapted to infecting humans as opposed to animals.*

***Transmission in animal models** is a measure of the ability of an influenza virus to transmit efficiently in animals in laboratory studies. Some influenza viruses can transmit through the air via small infectious droplets expelled through coughs or sneezes, whereas other influenza viruses may only spread through direct contact with an infected host.*

***Antiviral treatment options** refer to the predicted effectiveness of influenza antiviral medications, such as oseltamivir, zanamivir, baloxavir, and M2 blockers.*

Attributes of the Population category contains 3 of the 10 risk elements, including:

Population immunity refers to whether the human population has any existing immune protection against the novel influenza virus being evaluated.

Susceptibility to infection and severity of illness associated with specific influenza viruses may depend on age, geographic area, or genetic factors.

Disease severity and pathogenesis measure the severity of illness caused by a particular influenza virus in people and/or animals.

Antigenic relatedness is a measure of how similar an influenza virus not circulating in humans is to seasonal influenza vaccines, pre-pandemic candidate vaccine viruses, and stockpiled pre-pandemic vaccines.

Ecology and Epidemiology category contains the final 3 of 10 risk elements, including:

Global distribution in animals measures how widespread an influenza virus is in animals, the rate of spread over time, and any management factors that may affect the distributions.

Infections in animals refer to what kinds of animals are impacted by the influenza virus and the likelihood of human contact with these animals. For example, are influenza infections occurring in wild birds or domestic birds.

Human infections refer to evidence and frequency of human infections with an influenza virus not currently capable of sustained human-to-human transmission. If evidence exists, under what circumstances are human infections occurring? For example, how frequently and easily does transmission occur after direct and prolonged contact between humans and infected animals.

Viruses evaluated using the IRAT are listed on the CDC's website:¹⁰³ [Summary of Influenza Risk Assessment Tool \(IRAT\) Results](#). Extensive risk summaries are also included on the aforementioned CDC site. [Appendix C](#) includes links to additional information on each strain.

International Situations

WHO coordinates international aggregation and evaluation of influenza cases in humans, whether seasonal, newly emergent, or of zoonotic origin, though not without substantial support from CDC's international influenza efforts. CDC assists in strain evaluation, laboratory testing, vaccine determination, surveillance, epidemiology, and reporting of influenza internationally¹⁰⁴. For more information on how CDC supports international surveillance efforts, visit this site: [Influenza Division International Program \(cdc.gov\)](https://www.cdc.gov/influenza/division/international-program/).

For details on international tracking, reporting, and risk evaluation of influenza by WHO, go to the [International surveillance of human influenza virus activity](#) section of this document.

Influenza in Avian Species

Overview of Avian Influenza

Avian species play a significant role in the perpetuation of global influenza. Influenza A virus (IAV) is the only type of influenza that infects birds.¹⁹ The earliest isolation of an avian influenza virus was in 1961 in a tern in South Africa, followed by serologic evidence of infection in 1967.^{51,105} Avian influenza viruses (AIV) have played significant roles as the origin viruses for the 1918, 1957, and 1968 pandemics.⁵¹

Migratory waterfowl, particularly Anseriformes (ducks, mallards, or geese) and Charadriiformes (gulls and shorebirds), serve as reservoirs for IAV and rarely experience symptomatic infection.¹⁰⁶ Influenza viruses are most often spread between wild and domestic birds via the fecal-oral route, even among infected poultry. Ponds and rice fields in Asia are particularly ideal for this interaction, as are backyard poultry farms and live animal markets. Live animal markets provide a unique environment for rampant interspecies transmission as numerous bird types and mammals—from diverse backgrounds—capable of being infected with and spreading influenza viruses are brought together and housed in close proximity to one another prior to sale.¹⁰⁷

Domestic ducks can replicate the majority of influenza A subtypes, especially low pathogenicity avian influenza (LPAI) viruses, with inapparent infection, similar to their wild duck counterparts. Domestic poultry and game birds (e.g., quail, chicken, turkeys) play an interesting role in influenza transmission. In addition to being infected and developing disease, they can serve as intermediary processing hosts or “mixing vessels” as they possess both human and avian receptors $\alpha 2,6$ and $\alpha 2,3$ responsible for viral attachment and entry into host cells.¹⁰⁸ This ability differs by bird species. The same mixing vessel capability is present in swine.¹⁰⁹ Turkeys are highly susceptible to influenza virus infection as they support the replication of most avian and mammalian influenza viruses.^{108,110,111} Chickens and other domestic poultry are also highly vulnerable to influenza virus infection and have perpetuated H3, H5, H7, and especially H9 subtypes.^{90,112-114}

Of greatest potential threat to human health are the A(H5) and A(H7) subtypes. While low pathogenic A(H5) and A(H7) are endemic in many countries, the potential exists for these strains to evolve into highly pathogenic variants capable of causing 100% mortality in poultry, with spread to humans resulting in up to 60% mortality in previous cases.^{24,114} From 2003-2020, A(H5N1) highly pathogenic avian influenza (HPAI) viruses caused 861 human infections, of which 455 were fatal. While low pathogenic versions of these subtypes did not initially pose threats to human health, an increasing number of human infections causing severe illness and death in up to 25% of cases have been reported in the last 10 years.^{99,115} Since 2013, A(H7N9) LPAI has caused 1,568 human

cases, of which 616 were fatal. Another LPAI strain, A(H9N2), which is endemic in Africa, Europe, and Asia, resulted in 21 human cases in 2021, the most ever reported for that strain.^{116,117}

For more information on the role of IAV in avian species, see [Influenza A Virus](#).

Avian Subspecies Differentiation

Wild Waterfowl

The main species of wild waterfowl serving as reservoirs for IAV are Anseriformes (e.g., ducks, geese, and swans) and Charadriiformes (e.g., gulls, terns, and shorebirds).^{24,118} Infection and excretion in these species occur in the intestinal tract, with an exceptionally large concentration of virus excreted in their feces. However, the development of disease and symptoms occurs in the respiratory tract.^{24,28,50}

Wild Terrestrial Avian

Primary species studied with regard to influenza include quail and wild turkeys ^{24,108,109} Strains detected include A(H7) and A(H9) viruses.^{109,119,120}

Domestic Poultry

Primary species studied with regard to influenza include chickens, turkeys, and ducks. Commonly circulating subtypes include H5, H7, and H9, though strain and subtype vary widely by global region.

Highly Pathogenic and Low Pathogenic Avian Influenza

Avian influenza viruses (AIV) are categorized into 2 groups: low pathogenic avian influenza (LPAI) viruses and highly pathogenic avian influenza (HPAI) viruses. The differentiation between highly pathogenic and low pathogenicity is related to the virus's ability to cause illness and death in domestic poultry and does not refer to the severity of illness in humans. Both HPAI and LPAI have caused serious illnesses in humans.¹¹

Wild waterfowl are known to be the reservoir for all AIV; HPAI is thought to evolve in domestic poultry after transmission of LPAI from wild birds to poultry.^{14,24,121} After domestic birds are infected, a change in the hemagglutinin (HA) gene can occur allowing the virus to mature in the respiratory tract and cause systemic infection.^{24,52,122} The virus can also infect the gastrointestinal tract of birds, with minimal issues.⁸⁴ Once developed in poultry, HPAI can be transmitted back to wild birds. At present, HPAI is limited to A(H5) and A(H7) subtypes.^{24,51} Most AIV cause a gastrointestinal infection in birds with minimal clinical signs and are classified as low pathogenic.

The definition of infection with avian influenza according to OIE, 2016 is the following:¹²²

For the purposes of the Terrestrial Code, avian influenza is defined as an infection of poultry caused by any influenza A virus of the A(H5) or A(H7) subtypes or by any influenza A virus with an intravenous pathogenicity index (IVPI) greater than 1.2 (or as an alternative at least 75% mortality) as described below. These viruses are divided into high pathogenicity avian influenza viruses and low pathogenicity avian influenza viruses:

- a. *High pathogenicity avian influenza viruses have an intravenous pathogenicity index (IVPI) in six-week-old chickens greater than 1.2 or, as an alternative, cause at least 75% mortality in four- to eight-week-old chickens infected intravenously. A(H5) and A(H7) viruses which do not have an IVPI of greater than 1.2 or cause less than 75% mortality in an intravenous lethality test should be sequenced to determine whether multiple basic amino acids are present at the cleavage site of the haemagglutinin molecule (HA0); if the amino acid motif is similar to that observed for other high pathogenicity avian influenza isolates, the isolate being tested should be considered as high pathogenicity avian influenza virus.*
- b. *Low pathogenicity avian influenza viruses are all influenza A viruses of A(H5) and A(H7) subtypes that are not (or do not meet the criteria of) high pathogenicity avian influenza viruses.*

It is important to note that the OIE definitions for HPAI and LPAI do not explicitly include A(H9). LPAI A(H9) is a significant contributor to the global burden of influenza in domestic birds as well as increasingly in humans.⁸⁴

HPAI was first identified in 1996 in wild birds in China.^{24,123} The first case of human infection was detected in 1997 in Hong Kong.⁹⁰ The impact of vaccination, strain evolution, and poultry immunologic adaptation from exposure has reduced poultry morbidity and mortality in recent years. Occasional symptomatic outbreaks of HPAI happen among wild bird reservoirs, and infection in wild birds has increased in recent years.^{12,124} HPAI viruses do not circulate widely among wild birds, and they are not an established lineage circulating in poultry.¹² However, A(H5) LPAI, which is often the precursor to HPAI emergence, has been identified worldwide in wild birds and poultry.¹² Direct contact appears to be the most efficient method of transmission among infected poultry, though transmission most often occurs via fecal contamination of water ingested by uninfected animals; airborne transmission occurs less commonly.^{113,125}

As of May 2022, HPAI Eurasian clade 2.3.4.4b A(H5N1) has been detected in hundreds of wild birds in 38 states. This outbreak is significantly affecting the poultry industry with 34 states affected and over 37 million birds far exceeding the outbreak in 2014-2015.^{126,127} See [this section](#) for more information.

Lineage Distinctions

AIVs are often described as deriving from distinct geographic lineages. When introduced to a new region of the world, these viruses often reassort, acquiring genes from locally circulating viruses. Those regional or continental reassortant viruses then develop into their own lineages. These broad geographic classifications are further broken down by species and time period.⁴ Early AIVs detected in Asia are considered part of the Asian lineage, which led to a Eurasian lineage combining Asian and European genes. A North American lineage A(H5) virus was identified in 2004 and later diverged into “wild bird” and “poultry” lineages.^{9,14} There are additional supporting lineages named for viruses found in Australia and South America.^{128,129} North American lineage viruses have not yet been reported in humans.

Avian Influenza A(H7) Viruses: Asian Lineage

Within the subtype of A(H7) avian influenza Asian lineage, A(H7N9) low pathogenic viruses have caused the greatest number of human infections, primarily in China. A novel LPAI A(H7N9) virus emerged in China in 2013 causing 6 consecutive epidemic waves of human infection for a total of 1,568 cases and 616 deaths.^{24,130} The most severe wave occurred in 2016-2017 with 759 human cases.¹³¹⁻¹³³ Limited, unsustainable person-to-person transmission was reported.⁶⁷

In 2016, A(H7N9) avian viruses developed highly pathogenic capabilities. A total of 32 human infections were detected with HPAI virus, later sequenced in poultry, which was the likely source of human infection.^{134,135} A large-scale poultry vaccination program was implemented in China in September 2017 for A(H5) and A(H7) lineages, after which only 3 human cases of A(H7N9) were reported.^{67,136} The Asian lineage A(H7N9) viruses (both those with low and high pathogenicity) are believed to have the greatest pandemic potential if the virus were to achieve sustained person-to-person transmission.¹³⁶

Evolution of Avian Influenza A(H5) HPAI Viruses

At the end of the 19th century and beginning of the 20th century, outbreaks of what was likely highly pathogenic avian influenza were reported in chickens in multiple countries. However, for nearly a century thereafter, influenza outbreaks in poultry were rare and had limited spread. Outbreaks of influenza were more common in turkeys, as they were often raised in fewer enclosures and more open range than chickens. Turkey management practices changed because of the threat of avian influenza and

resulted in the now-widespread use of enclosures, thereby reducing the number of outbreaks in turkeys.¹³⁷ Genetic characterization or subtyping was not widely available on samples from wild or domestic bird outbreaks before 1990.

Highly Pathogenic Avian Influenza Emergence in Asia

In 1996, a unique lineage of A(H5N1) was detected in domestic geese in China.^{24,123,138} The A(H5N1) strain was designated as A/goose/Guangdong/1/1996 or Gs/GD A(H5N1) and is part of the Asian lineage of AIV.^{90,139} In the years after its discovery, HPAI continued to cause outbreaks in domestic poultry, resulting in almost 100% morbidity and high mortality despite massive, multiyear efforts to contain the virus. For the first 7 years following its discovery, HPAI A(H5N1) remained within China, then spread to 8 other countries in Asia by 2004, to Europe in 2005, and to Africa in 2006 (Figure 5).¹⁴⁰

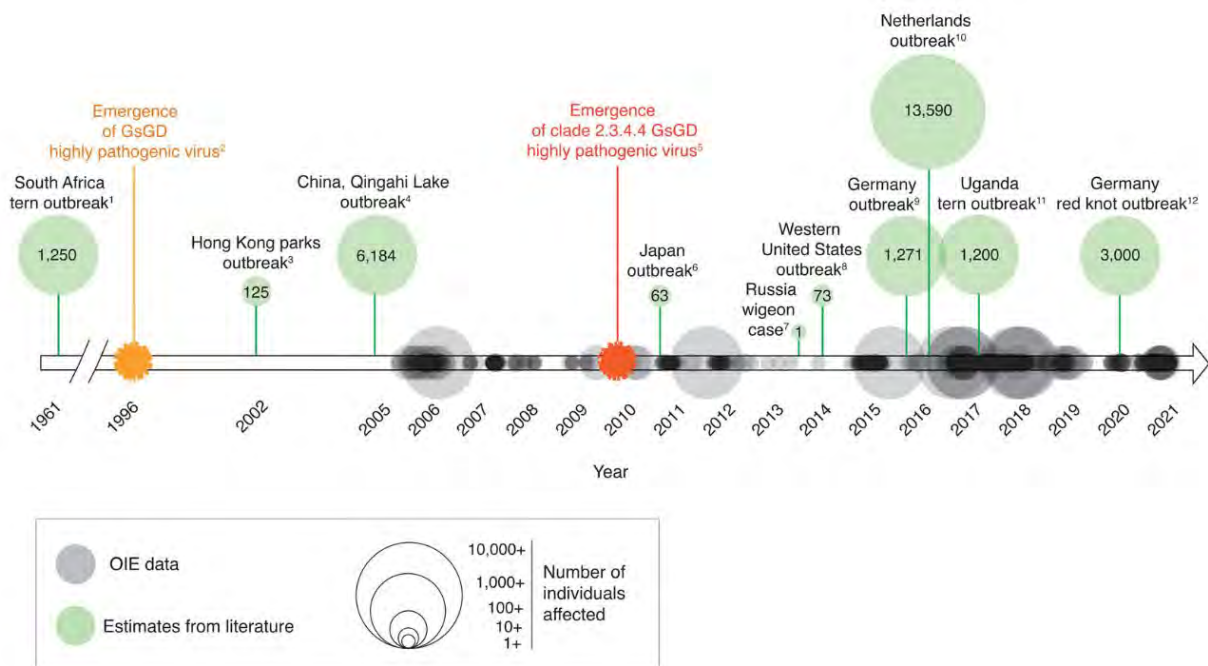


Figure 5. Timeline of magnitude and occurrence of highly pathogenic avian influenza (HPAI). Ramey, et al., 2021¹²⁴

In 2005, an outbreak of Gs/GD A(H5N1) resulted in the deaths of more than 6,000 wild aquatic birds.¹⁴¹ That same year, the virus was detected in wild birds in Europe.²⁴ From 2006-2009, an additional 38 countries detected Gs/Gd lineage A(H5N1) in domestic and wild birds, with different clades developing in different countries (Figure 4, Figure 5).^{84,142}

Sporadic outbreaks of Eurasian and Asian lineage A(H5) viruses among wild and domestic birds continued in Asia and Europe from 2010-2013.¹⁴³⁻¹⁴⁵ In 2010, a

genetically distinct clade 2.3.4.4 Gs/GD A(H5N1) lineage HPAI virus emerged, resulting in increasing occurrence of HPAI in wild birds (Figure 6).¹⁴⁶ The clade 2.3.4.4 virus became better adapted to waterfowl and was then able to cause asymptomatic infections in wild birds.¹⁴⁷

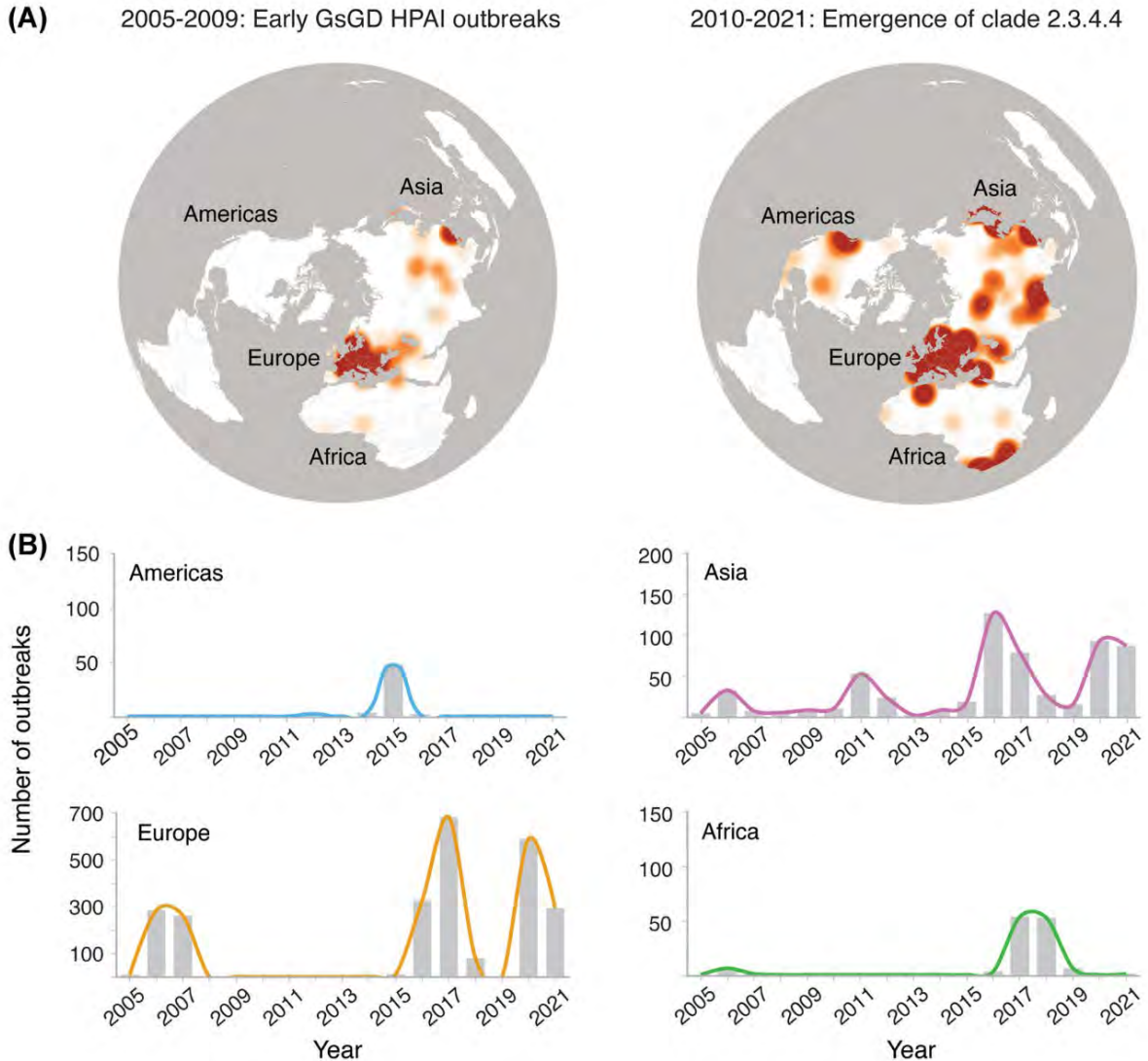


Figure 6. Occurrence of outbreaks of highly pathogenic avian influenza (HPAI) by world region and frequency, Ramey, et al., 2021¹²⁴

Highly Pathogenic Avian Influenza Emergence in North America

This first instance of HPAI in North America was an A(H5N2) subtype detected in Canada in chicken and turkey farms in 2014 (Figure 6). Not long afterward, another outbreak among birds was found in the state of Washington, close to the outbreak in Canada. The A(H5N2) virus in Canada was highly similar to the strain found in Washington.¹⁴⁸

The incursion of HPAI into North America in 2014 was remarkable because the A(H5N2) virus was related to the Eurasian lineage HPAI A(H5N8) virus. The A(H5N2) virus was also most likely spread from wild migratory birds (evidencing survivability throughout lengthy migrations) and was seemingly introduced to North America independent of a simultaneous outbreak in Europe.^{66,148,149} This event was also the first time that surveillance detected a Eurasian HPAI A(H5N8) that had reassorted with a low pathogenic North American AIV. Genetic analysis confirmed that reassortment had occurred between Eurasian and North American strains as the A(H5N2) virus contained Eurasian-origin HA plus 4 other Eurasian genes and North American wild bird lineage neuraminidase (NA) and PB1 genes.^{148,149}

Throughout 2015, the outbreak spread to wild waterfowl, chickens, and turkeys throughout the western and central United States and Canada.¹⁵⁰ It took almost 2 years until the outbreak of A(H5N2) was contained in North America, requiring the culling of 48 million birds and an estimated economic loss of more than \$3 billion.^{96,149,151} Following this outbreak in North America, A(H5N2) and closely related viruses became part of the North American lineage, which thus far has not caused human infection.

Outbreaks continued in Asia and Europe, and occasionally in Africa, after 2015 affecting wild birds and domestic poultry. Some outbreaks have caused significant mortality in birds (exceeding 10,000); also notable is the diversity of species and subtypes that can be infected with 2.3.4.4 Gs/GD H5Nx, which now includes gray seals, harbor seals, and red foxes.^{1,152,153} Thus far, HPAI has not been reported in Australia or South America.^{154,155}

Smith et al¹⁴⁶ provide additional detail on nomenclature and evolution of A(H5) clades from 2005 to 2012.

See [Appendix A](#) for a complete list of avian A(H5) outbreaks from 2005-2021.

LPAI Avian Influenza Subtype Summaries

A(H7N9)

Asian lineage A(H7N9) has a tropism for human and avian cellular receptors (humans α 2,6- linked sialic acid; avian α 2,3-linked sialic acid), thereby causing widespread waves of illness in birds and significant case counts in humans, with a ~39% mortality rate.^{135,141}

Identified in birds in 2013, this strain has caused 114 outbreaks affecting nearly 200,000 birds, primarily in China. Studies support the possible reassortment of A(H7N3) HA, A(H7N9) NA, and the remainder of genes from A(H9N2) avian viruses,

though the NA gene may have been acquired through reassortment from a Czech Republic virus.^{156,157} China experienced 6 epidemic waves of A(H7N9) from 2013 to present, despite aggressive vaccination and culling campaigns in birds.¹³⁶

In 2017, a North American lineage LPAI A(H7N9) strain was identified in poultry in Georgia, Tennessee, Alabama, and Kentucky along with a highly pathogenic A(H7N9) virus of the same lineage.¹⁵⁸

With regard to the Asian lineage and before 2013, A(H7) viruses primarily caused conjunctivitis in humans. With mutations acquired during avian outbreaks from 2013-2017, this strain caused 1,568 human infections in 3 countries and 616 deaths. Since 2017, only 3 human cases have been reported.¹⁵⁹

Influenza Risk Assessment Tool (IRAT)

To provide a frame of reference for the potential threat of various zoonotic influenza strains, findings from the Influenza Risk Assessment Tool (IRAT) are provided. The IRAT is used to evaluate the risk posed by animal influenza viruses potentially capable of spreading to humans. The risk of “emergence” and “public health impact” factors are assessed by federal, state, and local agencies involved in influenza incident investigations, and are coordinated by CDC. The “Summary Score” provides the category of cumulative pandemic potential, with higher scores in “Potential Emergence” and “Potential Impact” indicating higher risk.^{102,103}

Four A(H7N9) strains, both Asian and North American lineages, were evaluated using the CDC IRAT.¹⁰² The findings are displayed in Table 1.

Table 1. A(H7N9) avian influenza virus strains and their threat to human health, as evaluated by the Centers for Disease Control and Prevention Influenza Risk Assessment Tool¹⁰²

Influenza Strain	Date	Potential Emergence	Potential Impact	Summary Score
H7N9 [A/chicken/Tennessee/17-007431-3/2017]	2017	3.1	3.5	Low
H7N9 [A/chicken/Tennessee /17-007147-2/2017]	2017	2.8	3.5	Low
H7N9 [A/Hong Kong/125/2017]	2017	6.5	7.5	Moderate-high
H7N9 [A/Shanghai/02/2013]	2016	6.4	7.2	Moderate-high

A(H7N2)

In 2003, a human case of A(H7N2) was reported in New York. The case had no known poultry exposure.¹⁶⁰

In 2007, a cluster of human cases was identified in people with exposure to infected poultry at a public market in the United Kingdom. Limited person-to-person spread of conjunctivitis was reported.¹⁶¹

While not related to an avian exposure, a case of avian-like A(H7N2) was identified in a person with exposure to infected cats in an animal shelter in 2016, and later a second case associated with this event was found by serologic testing.¹⁶² Cats are not known to routinely circulate influenza viruses.

A(H7N3)

In 2002, LPAI A(H7N3) was detected first in Italy and then in the Netherlands, and in British Columbia in 2004 (HPAI was also detected).^{145,163} The outbreak in British Columbia affected approximately 600 commercial poultry farms, resulting in the depopulation of 19 million birds.¹⁶³ A total of 77 symptomatic human cases were reported with no hospitalizations or deaths. This was the first instance of human infection with A(H7N3).¹⁶³

A(H6N1)

A(H6N1) is one of the most common avian influenza viruses in wild and domestic birds. It was first detected in humans in 2013 in Taiwan. This strain poses a potential threat to human health as evidenced by its ability to reassort with A(H5N2) AIV while retaining its internal genes. This combination could improve its ability to infect humans.¹⁶⁴

A(H9N2)

The most widely circulating LPAI in the world, this strain is primarily isolated from domestic poultry and live bird market environments. A(H9N2) is frequently cited as the source of internal genes obtained by A(H5), A(H7), and A(H10) strains in reassortment events.

A(H9N2) was first isolated in Wisconsin in 1966 and caused sporadic outbreaks in the United States and Europe until the early 1990s. Since then, the strain has become endemic in domestic poultry in Asia, the Middle East, and Africa.¹⁶⁵ A(H9N2) viruses are often found cocirculating with A(H5) and A(H7) viruses, which has resulted in the acquisition of A(H9N2) internal genes by A(H5) and A(H7) strains.¹⁶⁵ A(H9N2) is believed to have supplied the non-HA and NA genes comprising the A(H7N9) LPAI virus that started waves of human and animal infection in China in 2013.^{14,157} The virus is split into 2 broad branches: the Eurasian and American lineages.

A(H9N2) has the ability to infect multiple species including minor poultry species (e.g., quail, pheasants), swine, canine, ferrets, pikas, and bats.^{114,166-170}

Early human infections prior to 1998 were asymptomatic and detected only through serologic surveillance.^{171,172} As of 2019, 59 human infections and 1 death have been reported with the majority occurring since 2015 (Figure 7). Cases are concentrated in children younger than 9 years.¹⁶⁵ Two A(H9N2) strains have been assessed using the CDC IRAT; a strain from Bangladesh in 2014 and Jiangxi-Donghu in 2014. Both were designated as “moderate” risk.¹⁰³

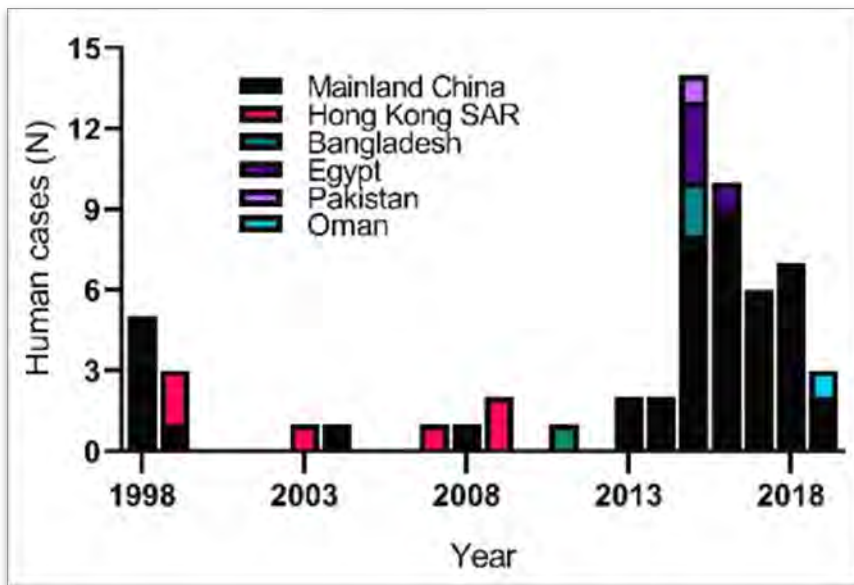


Figure 7. Human cases of A(H9N2), 1998-2019. Peacock, et al., 2019¹⁶⁵

A(H10N7)

A(H10N7) causes occasional outbreaks in poultry. Human infections with the strain are rare. In 2004, 2 infants were reportedly infected with A(H10N7) in Egypt. Their father was a poultry merchant who traveled regularly.¹⁷³ In 2012, 2 cases were confirmed in abattoir workers who had conjunctivitis and minor respiratory symptoms, though 7 other workers had symptoms of illness and did not test positive.¹⁷⁴ Outbreaks were also reported in harbor seals in 2015.¹⁷⁵

A(H10N8)

In 2013, 3 human cases of H10N8 were reported in China. The strain was identified in poultry from a live poultry market where they likely acquired infection.¹⁷⁶ Several studies have shown that internal genes of the H10N8 and other LPAI viruses like A(H5N1) and A(H7N9) are reacquired from A(H9N2) viruses.^{119,130,177} This strain was evaluated with the IRAT and determined to be of “moderate” risk.¹⁰³

HPAI Avian Influenza Subtype Summaries

A(H5N1)

Avian

A(H5N1) was not a noted threat to animal or human health until the 1996 emergence of the Gs/GD-lineage in Hong Kong in birds. The first human infection was identified less than a year later.^{90,178} While concentrated in China for 7 years after 1996, the Gs/GD-lineage A(H5) HPAI virus expanded its reach to other countries and continents after 2002.⁹⁰

The Gs/GD-lineage A(H5) HPAI rapidly became a major panzootic, the first among HPAI noted for its geographic spread and diversity in species affected. This strain was found in a wide range of wild and domestic birds and in some mammals including felines, canines, and others.^{179,180}

Although the original Hong Kong strain found in 1996 was quickly eradicated in Hong Kong, other A(H5N1) HPAI persisted, causing sporadic outbreaks between 2001 and 2003.^{181,182} In late 2003, nearly simultaneous outbreaks in domestic poultry occurred in 8 Asian countries (China, Cambodia, Thailand, Japan, Korea, Indonesia, Lao PDR, and Vietnam). Thailand and Vietnam experienced the most severe economic impact; more than 100 million birds were culled or died and there were multiple fatal human cases.¹⁸³ After 2004, a closely related sublineage of A(H5N1) (clade 2.2) was detected in migratory birds.¹⁸⁴ For years following, related viruses circulated in Russia, the Middle East, Europe, and Africa.¹⁸⁵

The Gs/GD-lineage A(H5) HPAI virus has been reported in more than 66 countries since 2003. In humans, A(H5) activity has decreased in recent years, having been replaced by other AIV subtypes.^{9,117} A(H5) HPAI continues to cause increasing outbreaks in wild and domestic birds.¹⁸⁶

Humans

Since 2003, more than 800 cases of A(H5N1) and more than 400 deaths have been reported in 16 countries (Figure 8).^{6,178} This virus is particularly virulent in humans, causing severe pneumonia and death in 50% of cases.⁶⁶ Nearly 500 cases were reported between 2003 and 2009 focused heavily in Asia, though present in Africa as well.¹⁸⁷ In the past 10 years, human infections with A(H5N1) have declined as other AIV subtypes become more prevalent, such as A(H5N6) and A(H9N2) viruses.^{187,188} While the World Health Organization requires reporting of any novel IAV with the capacity to infect a human, cumulative tracking is only published for A(H5N1). [ProMed](#) provides near-real-time reporting of cases from countries of origin.¹⁸⁹ Human cases exhibit some seasonality, with incidence peaks aligning with seasonal epidemics in poultry in

winter months, likely attributable to the timing of migrations and to increased domestic poultry production and consumption during the Lunar New Year in Asia.^{84,190}

H5N1 virus affects children and adults; not all human cases have had documented exposure to birds though 90% of those that did not were in clusters of family members.⁵² The median age of infected individuals through 2013 was 18 years, with 89% younger than 40 years.²⁴ The overall mortality rate in symptomatic, laboratory-confirmed cases is approximately 50% (Figure 8).¹⁷⁸ Seroprevalence studies suggest the overall risk of transmission from birds to humans is low, except for those with prolonged, unprotected exposure to known infected birds.²⁴

Two A(H5N1) viruses have been evaluated using the CDC IRAT: A(H5N1) clade 1 Vietnam virus in 2011 rated as “moderate” risk and a A(H5N1) Washington virus in 2015 rated as “low-moderate” risk.¹⁰³

Additional information about recent AIV infections in humans is located in the [Surveillance and Epidemiology](#) section of this guide.

Country	2003-2009*		2010-2014*		2015-2019*		2020		2021		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	6	1	1	0	0	0	0	0	8	1
Cambodia	9	7	47	30	0	0	0	0	0	0	56	37
Canada	0	0	1	1	0	0	0	0	0	0	1	1
China	38	25	9	5	6	1	0	0	0	0	53	31
Djibouti	1	0	0	0	0	0	0	0	0	0	1	0
Egypt	90	27	120	50	149	43	0	0	0	0	359	120
India	0	0	0	0	0	0	0	0	1	1	1	1
Indonesia	162	134	35	31	3	3	0	0	0	0	200	168
Iraq	3	2	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	2	2	0	0	0	0	1	0	0	0	3	2
Myanmar	1	0	0	0	0	0	0	0	0	0	1	0
Nepal	0	0	0	0	1	1	0	0	0	0	1	1
Nigeria	1	1	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	3	1
Thailand	25	17	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	12	4
Viet Nam	112	57	15	7	0	0	0	0	0	0	127	64
Total	468	282	233	125	160	48	1	0	0	0	863	456

Figure 8. Cumulative human cases of avian influenza A(H5N1) virus, 2003-2021. WHO, 2021.¹⁸⁷

A(H5N2)

One of the earliest reported A(H5N2) outbreaks was reported in Mexico among poultry flocks. The outbreak extended 15 months from 1993 to 1995.¹²¹ Outbreaks of

A(H5N2) emerged in France in 2003 and South Africa in 2004 while recurring outbreaks took hold in Asia.^{14,142} Between 2012 and 2019, the number of outbreaks and cases grew substantially among poultry to a peak of > 1 million cases in 2015, mainly in Asia; slightly surging again in 2017-2019.¹⁸⁶

An HPAI A(H5N2) outbreak was identified in ostriches in South Africa in 2011-2012, which also involved H7N1. Serologic surveys of people with known interactions with sick ostriches revealed 3 A(H5N2) positive cases over 2 years. The survey included testing for H7N1, which found 12 people seropositive for the virus.⁹⁹

In 2014, the first major outbreak of HPAI A(H5N2) virus in the United States was identified in turkey farms in Iowa, Minnesota, North Dakota, South Dakota, Wisconsin, and eventually several other states.^{67,148,149} The outbreak spanned more than 2 years and resulted in the culling of nearly 50 million birds at an industry cost of more than \$3 billion.^{96,149,150} Wild birds tested along the Pacific flyway were positive for A(H5N2) and A(H5N8) viruses.^{191,192} Genetic analysis revealed that a reassortment of the A(H5N2) (North American lineage) and A(H5N8) (Eurasian lineage) viruses was the cause of this North American outbreak.^{148,193} This virus (A(H5N2) A/Northernpintail/Washington) was evaluated using the CDC IRAT as “low-moderate” risk.¹⁰³

Additional details on the [emergence of A\(H5N2\)](#) in North America are located earlier in this document.

A(H5N6)

HPAI A(H5N6) has circulated in China since 2013, mainly in chickens and ducks. Outbreaks in 2014-2015 resulted in 3 human cases and 2 deaths, with all cases reporting direct contact with infected poultry in live bird markets.^{194,195} One study confirmed the presence of A(H5N6) (along with A(H7N9) and A(H9N2)) in air samples in affected markets.¹¹⁴ The 2013 Eurasian lineage HPAI A(H5N6) virus was a reassortant of A(H5N2) and A(H6N6).¹⁹⁴

In 2017, A(H5N6) was identified in 3 dead cats in China proximal to outbreak-affected poultry flocks.¹⁹⁶ In 2020, an outbreak was reported in migratory swans in China as the strain continued to circulate in chickens and ducks.¹⁹⁷

In 2016, a CDC IRAT of HPAI A(H5N6) determined the virus posed “moderate” risk in terms of pandemic potential. Due to the increase in cases reported by China in 2021, the IRAT was repeated, again scoring in the “moderate” risk category.¹⁰³ Of the 51 cases reported globally since 2014, 25 occurred in 2021. Most infected people had exposure to infected birds before becoming ill.¹⁹⁸

A(H5N8)

Outbreaks of A(H5N8) have been reported in birds since 1980.¹⁹⁹ However, in 2010, a novel reassortant HPAI A(H5N8) subclade 2.3.4.4b virus, evolving from the A(H5N1) clade 2.3.4, was detected in China in domestic ducks at a wet market.^{97,146,200} The virus remained in China until 2014 when outbreaks were detected in turkeys in South Korea and then in turkeys in Germany toward the end of that year.²⁰¹ Genetic analysis confirmed the German strain was closely related to that of Asia.

Since 2014, 2.3.4.4b viruses have spread to Africa and Europe via migratory flyways of wild birds, causing major European outbreaks in 2016-2017 and the introduction of HPAI A(H5N8) to North America in 2014.^{151,202,203}

A detailed account of the progression of A(H5N8) activity was provided by He et al⁹⁷ in 2021:

In early 2020, outbreaks of clade 2.3.4.4b viruses mainly occurred in Europe.²⁰⁴ Beginning in July 2020, several outbreaks of A(H5N8) viruses in poultry and wild birds were reported in Eurasia, including Kazakhstan, Russia, Poland, England, Netherlands, Korea, and Japan²⁰⁴⁻²⁰⁸; outbreaks were not reported in China until October 2020, when clade 2.3.4.4b viruses related to those circulating in Eurasia were detected in 2 dead swans in Mongolia.¹⁹⁷ Because eastern China is a major bird migration destination, migratory birds might carry HPAI viruses to this region. We detected 32 A(H5N8) viruses of 2 genetically distinct lineages in wild birds in eastern China.

Surveillance in migratory waterfowl in the Netherlands revealed that ducks likely served as continuous reservoirs for several years; detected viruses included A(H5N8), A(H5N5), and A(H5N1), all belonging to the 2.3.4.4b clade.²⁰⁴ Recent infections have been reported in seals, swans, and penguins.^{152,153,208} Transmission also occurred in a rehabilitation center in 2020 in the United Kingdom where swans were believed to have spread A(H5N8) to seals and a fox.²⁰⁹

In 2020, an outbreak of A(H5N8) in Russia was confirmed when approximately 100,000 birds died in December.^{199,210} Farmworkers were tested for serologic evidence of infection and 7 were positive. This is the first known instance of human infection with A(H5N8). The workers were not clinically ill, and there was no evidence of person-to-person spread. The strain belonged to the 2.3.4.4b clade originally detected in China in 2014. A CDC IRAT in 2021 determined the potential pandemic risk to be "moderate."¹⁰³

A(H7N3)

British Columbia experienced an outbreak of LPAI and HPAI A(H7N3) viruses in 2004.¹⁶³ The outbreak in British Columbia affected about 600 commercial poultry farms, resulting in the depopulation of 19 million birds.¹⁶³

From 2005 through 2021, outbreaks and cases occurred primarily in the Americas, with outbreaks sporadically reported in Europe, Asia, and Africa. Peak outbreak years in the Americas were 2012-2013, 2016, and 2019.¹⁸⁶

In 2012, Mexico reported outbreaks of HPAI A(H7N3) among domestic poultry. Two human cases of conjunctivitis were reported with known exposure to infected poultry.²¹¹

In 2018, surveillance at a Japanese airport detected a novel A(H7N3) virus in poultry meat that a passenger attempted to illegally smuggle from China. The strain was a reassortant of the A(H7N9) HPAI strain.¹¹²

A(H7N4)

This strain causes seemingly sporadic and likely undetected outbreaks. Since 2005, only 2 outbreaks have been reported, 1 in 2010 in the Netherlands and 1 in Cambodia in 2019.^{186,212} A 2-year surveillance along the East Asian-Australasian flyway confirmed the presence of A(H7N4) in migratory birds.²¹³

The first and only human case of A(H7N4) was identified in 2018 in a Chinese woman with exposure to poultry in a live bird market.²¹⁴

A(H7N7)

The earliest known transmission of HPAI from birds to humans was reportedly A(H7N7). In 1976, a laboratory worker accidentally splashed her face with A/chicken/Victoria/76, resulting in conjunctivitis.²¹⁵ In 1996, another human case of A(H7N7) conjunctivitis was identified in England in a woman who regularly interacted with feral ducks.¹¹⁰

In 1979, a mass mortality of more than 400 harbor seals was reported in Massachusetts, attributed to A(H7N7).²¹⁶

In 2003, an A(H7N7) outbreak in the Netherlands resulted in 453 reports of health complaints in poultry workers and their families. The most common clinical sign was

conjunctivitis, though 90 individuals had influenza-like symptoms. Of all those with illness, 89 were confirmed to have A(H7N7).²¹⁷

In 2013, an outbreak of A(H7N7) was reported in Italy, resulting in the depopulation of > 1 million birds. Three farm workers had laboratory-confirmed cases of conjunctivitis caused by exposure to infected birds.^{162,218}

A(H7N8)

In 2016, an outbreak of A(H7N8) was detected in the state of Indiana in turkey flocks. While originally LPAI, the virus is believed to have spontaneously mutated into HPAI. The index county for this outbreak shared a watershed with a large reservoir, which was frequented by wild migratory birds. Sustained increases in temperature and precipitation may have contributed to the viability of A(H7N8).²¹⁹⁻²²¹

A(H7N9)

North American lineage

This virus strain was first identified in the United States in 2017. Domestic poultry flocks infected with LPAI A(H7N9) virus were identified in Tennessee, Georgia, Alabama, and Kentucky.³ Exposure to wild birds was not confirmed by way of testing birds nearby; however, genetic sequencing indicates a source from wild birds.

Human illness due to A(H7N9) (North American lineage) has not been detected.

Asian lineage

First detected as LPAI A(H7N9) in 2013 in China, this lineage virus resulted in multiple consecutive waves of infections in people.¹³⁶ However, since 2017, and following a mass poultry vaccination campaign, only 3 human cases have been reported. For more information on this lineage, see the LPAI section of this guide A(H7N9).

A(H9N2)

In 1999, 2 human cases of influenza A(H9N2) were serologically detected in Hong Kong, evidencing prior infection.^{156,172} Human infection was again reported in China in 2018.²²²

A(H9N2) has been globally widespread among poultry for the past 2 decades.¹⁶⁵ Multiple outbreaks among swine have been reported, as well as infections in mink and bats.^{151,208} Several genetic studies suggest that internal genes for A(H5N6) and A(H3N2) viruses of feline and canine came from A(H9N2) viruses.^{168,223}

The A(H9N2) virus is hyperendemic in several countries and poses a threat to human health and the global poultry industry.¹⁶⁵ Recent surges in human cases support this threat. The CDC IRAT from 2014 for the G1 lineage A(H9N2) was rated as “moderate” risk, as was the Y280 lineage in 2019.¹⁰³

In 2021, the largest number of human infections with AIV A(H9N2) was reported, with most individuals linked to a live animal market. There was a total of 21 cases. Between 2015 and 2022, a total of 74 human cases and 2 deaths were reported by countries in the WHO Western Pacific Region.²²⁴

A(H10N3)

The first human case of A(H10N3) was reported by China in 2021. The individual had no clear contact with poultry, nor did local surroundings or nearby poultry confirm the presence of the virus.²²⁵

A(H10N8)

The first human infection with A(H10N8) was detected in a woman in China in 2013; transmission from a live animal market was the likely source of exposure.^{176,226} The strain was believed to be a novel reassortant, as it contained surface genes from Eurasian A(H10Nx) and North American A(HxN8) viruses found in wild birds, with all 6 internal genes from A(H9N2) found in poultry.¹¹⁹

A(H10N7)

In 2004, A(H10N7) was reported in 2 infants in Egypt who experienced illness with fever and cough. The father of 1 infant was a poultry merchant. The same virus was later isolated from 5 domestic ducks.¹⁷³

Influenza Viruses in Swine

Overview

Swine are known to routinely circulate influenza A viruses (IAVs), with peak circulation aligning with high levels of production, transportation, and marketing, though infection in swine is possible year-round.²¹ Outbreaks in swine and transmission to people occur most often in summer and fall at the time of agricultural fairs and shows. Common strains of swine influenza viruses (SIVs) include A(H1N1), A(H1N2), and A(H3N2).⁵⁰ Influenza A is endemic in swine populations in Asia, Europe, and North and South America.²²⁷

Classic swine influenza A(cH1N1) viruses were circulating in North American swine as early as 1930 but were not confirmed in European pigs until 1976.^{27,35} A shipment of pigs from the United States to Italy is believed to have resulted in the introduction of SIV to Europe.²²⁸ A few years later, the A(cH1N1) was replaced in Europe with a new avian-origin influenza A(H1N1) virus.^{5,76,229}

In the United States, A(cH1N1) continued to circulate without influence until 1998 when a triple reassortment event occurred.²⁷ Double reassortant swine viruses are defined as receiving genetic material from any 2 species infected with influenza, while the triple reassortant (tr) viruses contain genetic material from 3 species. In the rare situations in which this has occurred, as it did in 1998 and again in 2009, the resulting triple reassortant virus contained avian, swine, and human influenza genes and was designated A(trH1N1).²³⁰

Despite the widespread presence of IAVs in swine and frequent interactions between swine and humans over the last century, serologic evidence of human infection with SIVs was not identified until 1958, and it was not until 1974 that an SIV was isolated in a human.^{231,232} The incidence of human infection with SIV increased after the emergence of A(trH1N1) in 1998. From 1998 to 2009, there were 11 laboratory-confirmed cases of human infection with the triple reassortant virus in the United States; most patients reported exposure to swine prior to illness onset.²³³

It is important to note that the changes in A(H1N1) over the past 100 years involved different strains for people and swine (Figure 9). SIV cH1N1 differed from a previous human seasonal influenza A(H1N1). The pandemic A(H1N1) 1918 strain circulated seasonally in humans until abruptly disappearing in 1957.^{5,29} The A(H1N1) seasonal strain was replaced after the 1957 pandemic with a reassorted A(H1N2) virus. While likely influenced by the widespread presence of A(H1N1) in people, classical swine A(cH1N1) was confirmed in 1930, as previously mentioned.^{27,35} In 1977, an avian-origin A(H1N1) strain reemerged in Russia, causing an epidemic in people. There was

overlap with changes in swine influenza in Europe during the same period, as an avian-origin A(H1N1) virus also emerged in pigs.^{5,76,229} In 2009, the A(H1N1)pdm09 strain resulted in a pandemic, and the strain was different from A(cH1N1) and human seasonal A(H1N1).³⁵

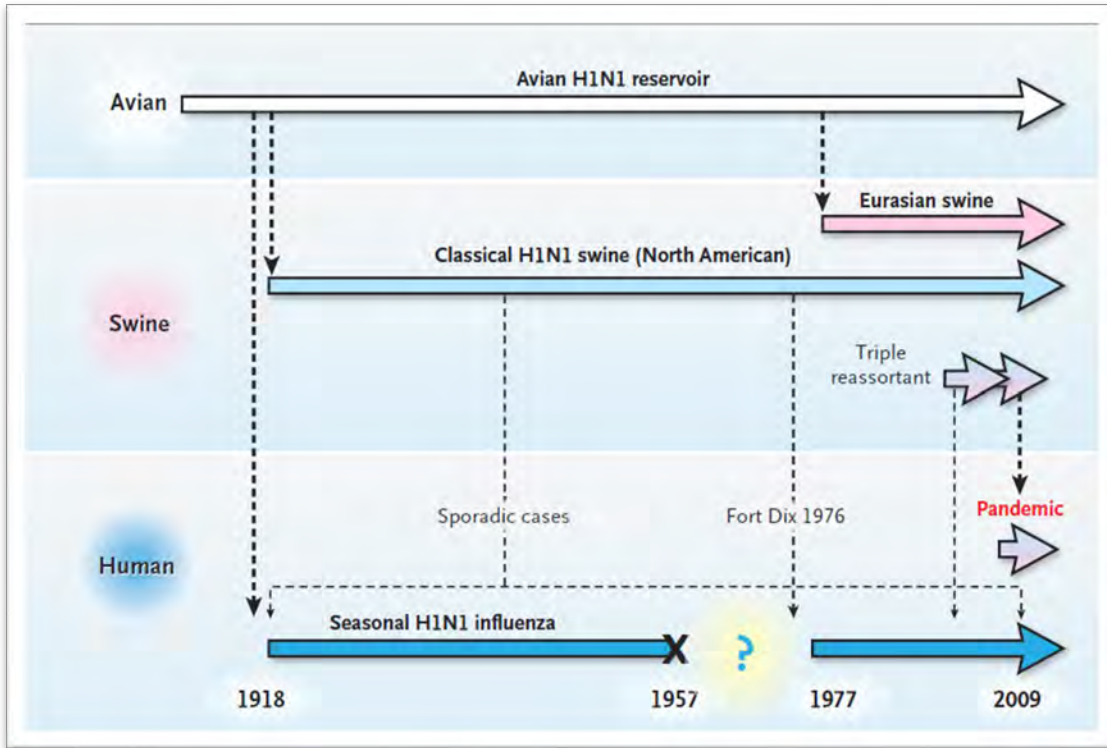


Figure 9. A(H1N1) viruses in avian, swine, and humans, 1918-2009. Zimmer & Burke, 2009.⁸⁰

Swine are often labeled as mixing vessels because they have both mammalian $\alpha 2,6$ and avian $\alpha 2,3$ receptors for IAVs in their tracheal epithelium.^{27,50} With a global population of approximately 677 million pigs, they have the potential to make significant contributions to influenza virus evolution and transmission; nearly 60% of global swine are in China.²³⁴ Any country, including China, with significant swine populations and proximity to poultry and humans has an increased chance for a novel swine strain to emerge. Poultry, wild birds, and several other animals including humans have the same mixing vessel ability, though quails are cited as a particularly effective intermediary host of avian influenza viruses (AIVs).^{108,235} Influenza viruses readily spread from humans to swine, perhaps more frequently than the reverse. Even in the 1918 pandemic and the A(H1N1)pdm09 pandemic, pig outbreaks temporally followed human outbreaks.^{5,30}

Clinical manifestation of influenza in pigs takes 1 of 3 forms: (1) a respiratory disease similar to human infection with cough, fatigue, fever, and nasal discharge for 3-7 days;

(2) as part of porcine respiratory complex acting with *Mycoplasma hyopneumoniae* and other bacterial pathogens of pneumonia; (3) no clinical signs of illness.^{21,24,27}

Swine Influenza Subtype Summaries

A(H1N1)pdm09

The A(H1N1)pdm09 pandemic of 2009 began in Mexico, although it was first identified in 2 children in San Diego, California, resulting in the strain being named for the state of discovery (A/California/04/2009).^{73,85} Genetic characterization and phylogenetic analysis suggest that A(H1N1)pdm09 was circulating in swine up to 1 to 2 years before its appearance in people.^{35,236} In addition, low genetic diversity suggests that the introduction to humans was a single event or a series of events with a similar virus.³⁵ The emergence of a swine-origin influenza pandemic was surprising as avian influenza outbreaks in poultry and sporadic human infections were increasing throughout Asia in the years preceding the A(H1N1)pdm09 influenza pandemic.²⁴ However, many precursor events in the United States evidenced increasing risk of interspecies transmission of influenza between swine and people.²³³

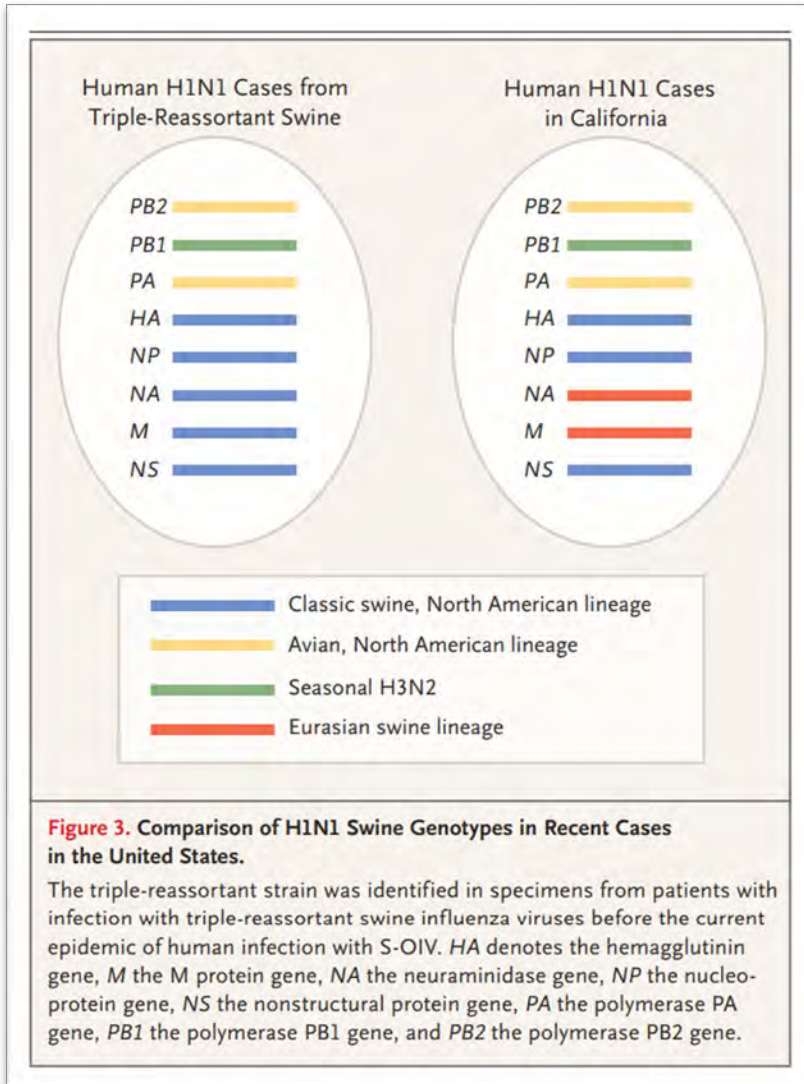


Figure 10. Comparison of human A(H1N1) cases from triple reassortant swine to human A(H1N1)pdm09 cases in California (Novel Swine-Origin Influenza A [H1N1] Virus Investigation Team, 2009).

The A(H1N1)pdm09 eight segmented genome had 4 primary origins. The neuraminidase (NA) and M genes were sourced from A(H3N2) Eurasian swine lineage viruses. The hemagglutinin (HA), NP, and NS genes were from classical SIVs of the North American lineage. The PB2 and PA genes were from North American lineage AIVs, and the PB1 gene originated from human seasonal A(H3N2) (Figure 10).³⁵

To summarize, the A(H1N1)pdm09 genome contained 6 gene segments (PB2, PB1, PA, HA, NP, and NS) previously found in triple-reassortant swine viruses circulating in pigs in North America.⁸⁵ The remaining 2 genes, NA and M, were closely related to SIV circulating in Eurasia. This combination was completely

new. Before A(H1N1)pdm09, the triple reassortant consisted of 4 genes from classical SIVs (including HA and NA), 2 from AIV (North American lineage), and 1 from human IAV. Triple reassortant swine virus was first identified in the United States in 1998.⁸⁵

The A(H1N1)pdm09 strain continues to circulate seasonally in swine and humans throughout the world.

trH1N1, trH1N2, trH3N2

Swine triple reassortant viruses are the main influenza viruses circulating among pigs in recent years.⁶⁵

A(H1N1)

Classical swine A(H1N1) or cH1N1 evolved from the 1918 Spanish flu, and while only 3 of 8 genes were related to the A(H1N1)pdm09 strain, the virus changed very little antigenically until 1998.^{33,237} The 1998 reassortment was the result of humans infecting pigs.²¹ Additional reassorting occurred that resulted in new genotypes of A(H1N1) and A(H1N2) retaining the triple reassortant internal genes.²³⁸ These strains represent almost 50% of circulating strains in swine in the United States.²³⁹

A(H1N2)

This strain was isolated in pigs in Japan in 1978 and in multiple other countries before its detection in the United States in 1997. This strain causes infrequent infections in humans.²⁴⁰

A(H2N2)

A(H2N2) circulates in swine and birds but has not been identified in a human in more than 40 years. This strain became a dominant seasonal strain after the pandemic in 1957, then dissipated in 1967.²⁴¹

A(H3N2)

SIV A(H3N2) is distinct from human seasonal A(H3N2) virus in that it normally circulates in pigs and causes sporadic human infections.²⁴² However, in 2011, a reassortment of SIV A(H3N2) was identified with the A(H1N1)pdm09 M gene. The acquisition of this gene may make SIV A(H3N2) more transmissible to humans. Although only 11 human cases of novel influenza from swine were reported from 1998-2009, 12 human cases were confirmed in 2011 alone, followed by a record 300 cases in 2012. The majority of these events, but not all, were attributed to an H3N2v, as displayed in Figure 11.

	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	Total
Influenza A H1N1v	0	2	2	0	3	1	0	1	1	0	8	0	18
Influenza A H1N2v	0	4	0	0	0	3	4	14	0	0	4	0	29
Influenza A H3N2v	7	315	20	3	3	19	61	2	0	1	2	1	434
Influenza A H7N2	0	0	0	0	0	0	1	0	0	0	0	0	1
Influenza A H1v	0	0	0	0	0	0	0	0	0	0	0	1	1
Total	7	321	22	3	6	23	66	17	1	1	14	2	463

Figure 11. US novel influenza A infections in humans. CDC Outbreaks, 2022.²⁴³

Infections in people continue to occur, usually resulting from prolonged exposure to pigs at agricultural fairs. Sustained person-to-person transmission has not yet occurred.^{239,244-248}

A(H4N6)

This wholly AIV was isolated from pigs experiencing an outbreak of respiratory disease in Canada in 1999. The farm where the outbreak occurred was located close to a lake frequented by migratory birds. Water from that lake was regularly given to pigs for drinking. Transmission of the avian virus from contaminated lake water to pigs, then pig to pig, was the confirmed route of exposure. This outbreak was also the first known instance of pig-to-pig spread of this AIV. Farm personnel were asymptomatic, though the serologic status of infection was not determined.²³⁷ Lack of evidence for A(H4N6) infections in pigs since 1999 suggests this may have been an isolated incident.

A(H5)

There are no reported events of swine-origin A(H5) strains of the influenza virus. However, when AIV infections have been detected in swine there appears to be no sustained onward transmission. This suggests that AIV infections may run their course in a swine population and are naturally eliminated.⁸⁴ Swine have cellular receptors for avian and mammalian influenza viruses, and avian A(H5) infections in pigs have occurred.^{27,50}

A(H6N6)

Identified in Southern China in 2011, this sporadic infection of A(H6N6) in pigs was believed to originate from ducks. This virus does not circulate widely in swine.²⁴⁹

A(H9N2)

A(H9N2) does not circulate in swine and is an AIV. This strain is not well-adapted to spread between pigs; however, that potential exists, as does the potential for human infection.

Influenza Viruses in Equine

Overview

Equine influenza virus (EIV) is a highly contagious common infection of horses, with historical documentation of incidence dating back centuries.²⁵⁰ Often overlooked outside of equine communities, outbreaks have disrupted horse racing and the show industry, as well as impacting those who rely on equids for income. Despite the availability of EIV vaccines and quarantine standards for the importation of horses, the international horse trade is a common source of large-scale outbreaks.²⁵¹ Periodic, significant outbreaks also occur in countries like Mongolia in nomadic horse herds where outbreaks affect associated economies.²⁵²

Equine influenza causes acute symptoms of infection including dry cough, lethargy, fever, nasal charge, and anorexia that typically resolve within 2 weeks.²⁵³ EIV is believed to have originated from avian influenza viruses. EIV can infect all equids, wild and domestic, including donkeys.^{254,255} EIV can spill over to dogs, cats, swine, and likely many other mammals. Transmission from horses to humans is possible. Humans can also infect horses with human influenza, though the subsequent infection in horses is usually asymptomatic.²⁵⁶ Elevated antibodies to EIV have been detected in humans in multiple EIV outbreaks.²⁵¹

A(H7N7)

A(H7N7) was first identified in horses in 1956 in Europe and was last identified in the 1970s, though serologic tests suggest that circulation ended in the 1990s.^{78,257}

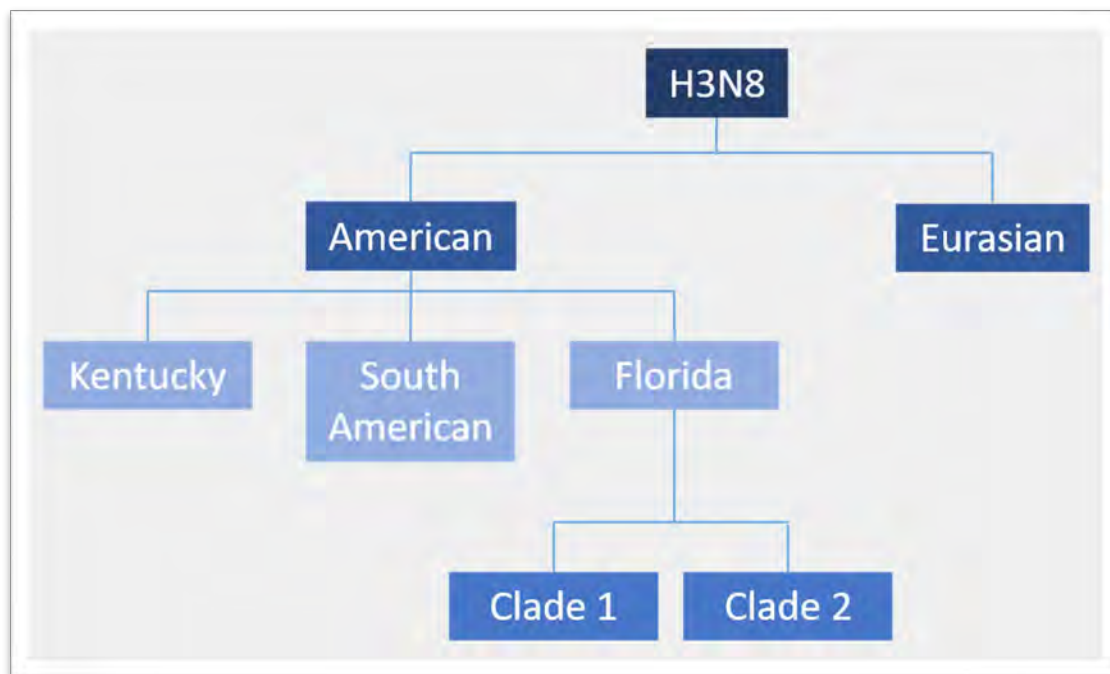


Figure 12. Equine influenza A(H3N8) virus American and Eurasian sub-lineages, University of California, Davis, 2019.⁷⁸

A(H3N8)

A(H3N8) has 2 distinct lineages: Eurasian and American. Eurasian lineage viruses have not been detected since 2007. The American lineage is more common today, with sublineages attributed to Florida, Kentucky, and South America. The Florida sublineage is further split into 2 clades, with clade 1 found in the United States and clade 2 in Europe (Figure 12).²⁵⁸⁻²⁶² Both Florida clades are currently recommended for inclusion in equine influenza vaccination, though the equine vaccine is intended to prevent illness, not infection. Therefore, previously vaccinated horses can experience transmissible subclinical infection.²⁶³

Outbreaks among horses are regularly detected in most countries except New Zealand and Iceland. Australia experienced a large outbreak in 2007 that affected more than 70,000 horses, with a 5% mortality rate. The cause of the outbreak was believed to be an importation from a thoroughbred from Japan whose illness was missed at an Australian quarantine station. The estimated cost of that outbreak exceeded \$1 billion.⁹⁸ Another significant, international outbreak started in Chile in 2011-2012 and spread to numerous countries.²⁵³

Influenza Viruses in Canine & Feline

Overview

Influenza A virus (IAV) is spread between and among dogs and cats through respiratory droplets and occasionally between the 2 species. As shown in Figure 13, periodic canine infections have diverse origins, including horses (equine-origin CIV is no longer circulating), birds, humans, and swine. Only canine influenza virus (CIV) A(H3N2) has adapted to dogs, though it was originally an avian strain.⁸⁴ Feline infections include low pathogenicity avian influenza (LPAI) A(H7N2) and highly pathogenic avian influenza (HPAI) A(H5N1) avian influenza viruses (AIVs). The A(H1N1)pdm09 strain infected both felines and canine.²⁶⁴

Influenza A subtype ^a	First isolation (localization and year)	Host species (origin)	Currently reported geographic distribution ^b	Severity of the disease ^c	Intraspecies transmissibility ^d	Transmission to humans ^e	References
CIV-H3N8	Florida, USA, 2004	Dogs (Horse)	USA ^b , UK, Canada	+	+	Never reported	(7–9)
CIV-H3N2	China, 2006	Dogs and Cats (Avian)	Southeast Asia ^b , North America ^b	++	++	Never reported	(10–16)
LPAIV H7N2	New York City, USA, 2016	Cats (Avian)	USA	+	+	Reported once	(17, 18)
HPAIV H5N1	Thailand, 2006	Dogs and Cats (Avian)	Thailand, China, Austria, Germany	+++	-/+	Never reported	(19–25)
A(H1N1)pdm09	Italy, 2009	Dogs and Cats (Human)	USA, China, Mexico, Italy	+++	+	Reverse zoonosis	(26–34)
CIV-H3N1*	South Korea, 2010	Dogs (Human)	Unknown	-	-	Never reported	(35)
CIV-H3N2*	South Korea, 2012	Dogs (Human)	Unknown	++	+	Never reported	(36)
CIV-H1N1r*	China, 2015	Dogs (Swine)	China	++	Unknown	Never reported	(37)
CIV-H1N2r*	China, 2014	Dogs (Swine)	China	+	Unknown	Never reported	(37)
CIV-H3N2r*	China, 2015	Dogs (Swine)	China	+	Unknown	Never reported	(37)

^aCIV, Canine Influenza Virus; HPAIV, High Pathogenic Avian Influenza Virus; pdm, pandemic; LPAIV, Low Pathogenic Avian Influenza Virus; r, reassortant and further highlighted by an asterisk.
^bRefers to endemic subtype in canine population.
^cSeverity was defined based on the following criteria: + mild respiratory symptoms; ++ severe respiratory symptoms; +++ systemic infection.
^dIntraspecies transmissibility refers to dog-to-dog and cat-to-cat transmission events and was classified as follows: - no evidence of case-to-case transmission; -/+ limited transmission; ++ efficient spreading.
^eReverse Zoonosis refers to an influenza subtype that can be transmitted from humans to companion animals.

Figure 13. Overview of major influenza A virus infections reported in dogs and cats. Borland, et al., 2020.²⁶⁴

Both dogs and cats contain receptors for both mammalian and avian IAVs (mammalian α 2,6-linked sialic acid; avian α 2,3-linked sialic acid), making them a potentially important link in interspecies transmission of influenza viruses.^{168,265} Multiple studies show that dogs may be infected with a variety of IAV strains, including A(H1N1)pdm09, and that strains from multiple species can reassort in dogs, which lends evidence to the possibility that dogs may be another “mixing vessel” species.^{264,266} Opportunities for reassortment are particularly evident in China because of the presence of free-roaming dogs and dogs farmed for meat production, as determined by surveillance in veterinary clinics of dogs with respiratory illness.²⁶⁷ Given their close proximity to humans, and their large global population (more than

700 million), dogs could play a larger role in zoonotic transmission of influenza viruses in the future.^{168,268,269} Despite the known presence of mammalian and avian influenza receptors in cats, they were not known to be a species in which reassortment of IAV took place until a detection event occurred in China in 2017.²²³

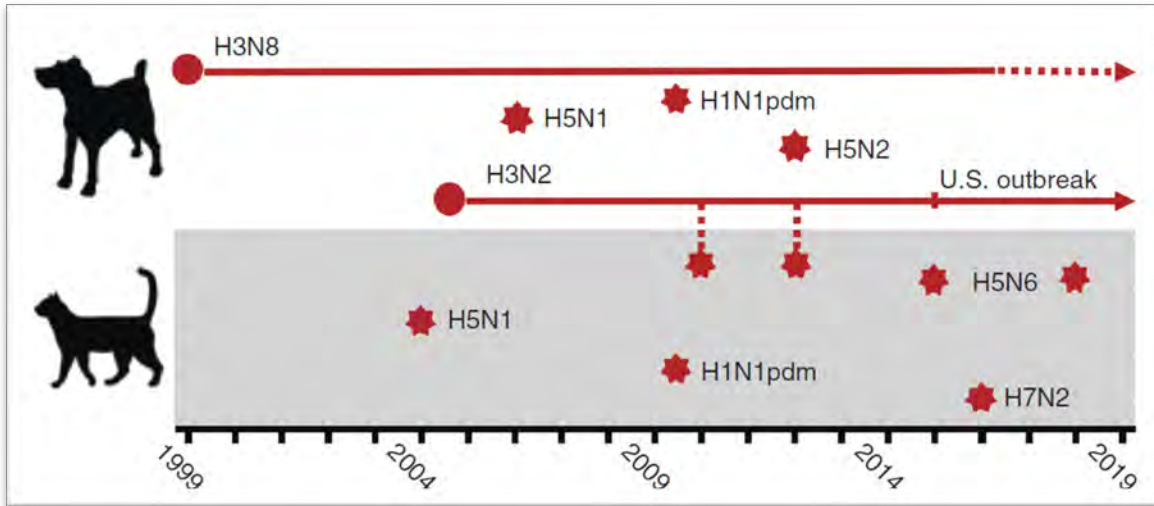


Figure 14. Canine and feline influenza A virus evolution from 1999-2019. Wasik, et al., 2021.²⁶⁶

The following is a description of Figure 14 from Wasik et al²⁶⁶ in 2019:

Timeline of major canine outbreaks as well as canine and feline spillover events since 1999. Outbreaks of equine-origin A(H3N8) and avian-origin A(H3N2) in dogs have been sustained in dog populations, with a major contraction (or possible resolution) of A(H3N8). Major spillover subtypes include A(H5N1), A(H5N2), A(H5N6), A(H7N2), and A(H1N1)pdm. Dog-to-cat cross-species transmissions have been observed with canine influenza virus (CIV) A(H3N2) in Korea.

Canine

A(H3N8)

A(H3N8) CIV emerged around 2000 from an EIV and was transmitted to dogs, as confirmed by serologic evidence. The A(H3N8) EIV was recognized 40 years earlier.²⁷⁰ In 2004, the CIV spread among greyhounds at a Florida race track and then spread rapidly throughout the United States, with continuing outbreaks in racing greyhounds in 11 states and animal shelters across the United States for the next 2 years.^{270,271} Around the time of the 2004 Florida outbreak, other outbreaks were noted in dogs in Australia, the United Kingdom, and South Korea.^{168,272,273}

At present, there is no evidence of transmission of A(H3N8) from canines to humans.²⁷⁴ CIV A(H3N8) circulated until around 2019 in the northeastern United States and

Colorado, mainly in animal shelters and kennels with a high turnover of animals.^{20,270} The lack of recent activity suggests possible extinction of this virus.²⁷⁵

A(H3N2)

CIV A(H3N2) appears to have originated in birds, then infected dogs, and now spreads between dogs.²⁰ The virus was first identified in dogs in South Korea in 2007, followed by reports of infected dogs in China, Thailand, and Canada. In 2015, this CIV A(H3N2) virus was confirmed in dogs in the United States. Following the 2015 introduction, an outbreak in Chicago in 2016 infecting more than 1,000 dogs resulted in sustained low-level transmission despite shelter control efforts.²⁷⁶ Although the original US outbreak died out, the virus is continually reintroduced by dogs imported from Asian countries where disease is endemic.^{277,278} Two outbreaks in Los Angeles County, California, were reported, one in 2017 and one in 2021, among shelter dogs.^{279,280}

Other Strains

In 2014-2015, swine influenza virus reassortant A(H1N1), A(H1N2), and A(H3N2) infections in dogs were reported in China.²⁶⁴

Feline

A(H1N1)pdm09

An outbreak of A(H1N1)pdm09 was reported in Italy in 2009 that infected and caused illness in more than 90 cats.²⁸¹ This outbreak confirmed the ability of influenza to spread between cats, though prior outbreaks with A(H5N1) supported this as well. Sporadic cases of A(H1N1)pdm09 were also reported in domestic cats in other countries, coinciding with surges in A(H1N1)pdm09 influenza activity in 2009 and beyond.^{266,281}

CIV A(H3N2)

Sporadic cases of CIV A(H3N2) have been reported in cats in Korea, though sustained transmission in feline populations has not occurred.^{207,282}

A(H5N1)

H5N1 A(H5N1) virus was the cause of an outbreak in domestic cats in 2004 in Thailand where at least 1 cat was known to have had contact with chickens. Infections in larger cats including tigers and leopards in a Thailand zoo were tied to tigers being fed infected chickens. There were some instances of assumed tiger-to-tiger transmission because not all of the sick tigers had consumed infected chicken.^{283,284} Studies involving field serosurveys show that prevalence of H5N1 A(H5N1) in cats is rare. Confirmed cases of feline influenza with A(H5N1) usually involve the interaction of cats

with a wild animal or domestic bird influenza outbreak or cat consumption of infected birds.^{283,285}

H5N6

Similar to A(H5N1) AIV, A(H5N6) AIV periodically infects cats. In 2014, a fatal infection in a feline followed a poultry and human outbreak in China. Two novel reassortant A(H5N6) viruses with A(H9N2) and A(H7N9) genes were identified in cats in 2016, also in China. In 2016-2017, additional cases in cats were confirmed during a poultry outbreak in South Korea where cats were in close proximity to an affected farm.²⁶⁶ Feline infections may have been acquired from interactions between domestic cats and wild birds, whether through cats feeding on infected birds or other direct contact.¹⁹⁶

A(H7N2)

A feline outbreak in a New York City animal shelter in 2016 was attributed to an LPAI A(H7N2) virus.^{286,287} Two human infections were confirmed, 1 in a veterinarian with mild symptoms and a second confirmed retrospectively with no symptoms reported. These were the first known human infections with A(H7N2).^{162,287}

Interspecies transmission risk

Because of the proximity of canines and felines in shelters, especially in the United States, the transmission of CIV to cats happens occasionally.²⁰⁷

Influenza Viruses in Bats

Overview

Despite their ability to harbor more life-threatening zoonoses than any other mammalian species, bats were not suspected as key players in influenza virus distribution until identified in Guatemala in 2009. This discovery was the result of a 2-year surveillance study to assess influenza virus prevalence in Guatemalan fruit bats.²⁸⁸

A new A(H17N10) subtype was discovered in 2012 in Central American fruit bats in Guatemala followed by the detection of A(H18N11) in fruit bats in Peru.^{288,289} Sequencing of the A(H18N11) virus revealed that it was phylogenetically close to A(H17N10) but had exceptionally divergent hemagglutinin (HA) and neuraminidase (NA) encoding sequences. This drew researchers to the conclusion that influenza had been present in bats for much longer than previously thought.^{17,289} These discoveries indicate the potential for widespread circulation among bats in the Americas; however, substantial genetic modification is likely necessary before bat influenza viruses could infect and spread among humans or other species.^{17,290} The internal genes of bat influenza virus strains are compatible with human influenza viruses but would require reassortment to acquire the requisite surface proteins for human infection.¹⁷

Infection with A(H18N11) has also been reported in the Brazilian free-tailed bat. A(H9) subtype antibodies have been found in frugivorous bats in Ghana, and the influenza A virus strain A(H9N2) was isolated from Egyptian fruit bats in 2019.²⁹¹⁻²⁹³

Influenza in Other Animals

Sea Mammals

Seals and other pinnipeds are susceptible to influenza A virus infection, likely resulting from onshore interactions with wild birds. Notable outbreaks among harbor seals include A(H7N7) in Cape Cod, Massachusetts, in 1980, A(H3N8) in the northeast United States in 2011, and A(H10N7) in Denmark and Sweden in 2014. Seals experience pneumonia from influenza virus infection that can cause significant mortality. Seals may also acquire influenza B virus infections from humans.^{15,175,216,294}

Ostriches

An outbreak of the highly pathogenic avian influenza (HPAI) A(H5N2) virus occurred in ostriches in Eastern Cape Province, South Africa, in 2004 linked to avian influenza virus carried by wild ducks.¹⁴ Two additional outbreaks of HPAI A(H5N2) were reported years later in nearby Western Cape Province, South Africa. The first was in 2011 and was attributed to an HPAI A(H5N2) virus, and the second in 2012 was caused by a low pathogenicity avian influenza (LPAI) A(H7N1) virus. Extensive serologic testing was conducted in nearly 400 people involved with outbreak mitigation in 2011 and 2012. Human infection with HPAI A(H5N2) virus from 2011 was confirmed in only 3 individuals, while 4 ostrich abattoir workers and 4 veterinarians had serologic evidence of LPAI A(H7N1) virus infection from 2012. Mild conjunctivitis symptoms were reported by 1 veterinarian at the time of the A(H7N1) outbreak, but the infection was not confirmed to be influenza.⁹⁹

Pandas

A single case of A(H1N1)pdm09 was detected in an asymptomatic panda in Hong Kong in November 2018.²²

Penguins

AIV A(H11N2) was detected in Adelie penguins in Antarctica in 2013. Genetic examination revealed diverse origins, though the majority of segments were from North American lineage viruses with neuraminidase (NA) genes derived from Eurasian lineages.²⁹⁵ AIV persisted in Antarctica, with continued detection of H11 subtype viruses in other penguin species. In 2015, a novel A(H5N2) virus was isolated in a chinstrap penguin; the virus was genetically similar to the A(H11) viruses already present on the continent.²⁹⁶ In 2019, an outbreak among African penguins on an island in Namibia, Africa, was reported. The AIV subtype was A(H5N8) and the strain had high similarity to an HPAI A(H5N8) subtype found in South Africa in 2017.¹⁵² These discoveries highlighted the persistence of influenza viruses, reassortment between lineages in Antarctica, and the potential for devastating introduction of HPAI viruses to the Antarctic penguin population.²⁹⁵

Ferrets

Ferrets are susceptible to infection with human influenza A viruses and share immunologic similarities; therefore, they are frequently used as a model for studying human influenza virus infection.²⁹⁷ Research investigating the role of wild or domesticated ferrets in influenza transmission is sparse.

Surveillance, Epidemiology, Prevention & Control of Influenza

The following sections outline domestic and international approaches to surveillance, the epidemiology of zoonotic influenza, transmission as well as ecological factors affecting transmission, prevention, and control. Similar to previous sections of this document, content is organized by species starting with human, then avian, followed by swine and other animals.

US and International Human and Animal Surveillance: Quick Reference

Table 2 provides quick references to major influenza surveillance systems, maps, and reports for humans and animals in the United States and internationally. The World Health Organization (WHO) aggregates cases of avian and swine infections in humans on a near-monthly basis in its Monthly Human-Animal Interface Reports.¹¹⁷ The following sections provide detail and context for these systems and also discuss the epidemiology, prevention, and control of seasonal and novel influenza virus infections in humans.

Table 2. Surveillance report references for human, avian, and swine influenza viruses, by US and international sources

Influenza Virus	United States	International
Human seasonal	Weekly U.S. Influenza Surveillance Report	FluNet (who.int) WHO Biweekly Global Influenza Update
Human novel (and variant) ^a	Novel influenza A virus infections (cdc.gov)	WHO FluMart Outputs Monthly human-animal interface reports: Global Influenza Programme (who.int) Cumulative number of human A(H5N1) cases: Global Influenza Programme (who.int)
Swine ^b		
Avian (poultry)	Highly pathogenic avian influenza (HPAI)	Avian Influenza—OIE—World Organisation for Animal Health OIE-World Animal Health Information System (WAHIS)
Avian (wild-terrestrial and aquatic)	WHISPers (usgs.gov) Avian influenza and wild birds Highly pathogenic avian influenza (HPAI)	
Outbreak reports	Highly pathogenic avian influenza (HPAI)	Disease Outbreak News (who.int) Influenza Research Database—Influenza genome database with visualization and analysis tools (fludb.org) The Weekly Epidemiological Record (WER) (who.int)

^a“Variant” influenza in the US refers to human infection with a swine influenza virus. Internationally, “novel” influenza refers to any influenza virus that undergoes molecular, antigenic, or genetic changes from the original virus, regardless of species.

^bInfluenza is endemic in swine and not actively surveyed at the national or international levels. Some national outbreaks are tracked by state and local health agencies and the US Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS).

Human Influenza Surveillance and Epidemiology

Human (Seasonal) Influenza Surveillance in the United States

According to the Centers for Disease Control and Prevention (CDC),²⁹⁸

The U.S. influenza surveillance system is a collaborative effort between CDC and its many partners in state, local, and territorial health departments, public health and clinical laboratories, vital statistics offices, healthcare providers, hospitals, clinics, emergency departments, and long-term care facilities. Information in five categories is collected from nine data sources in order to:

- *Find out when and where influenza activity is occurring;*
- *Determine what influenza viruses are circulating;*
- *Detect genetic changes in influenza viruses; and*
- *Measure the impact influenza is having on illness, hospitalizations, and deaths.*

The core components of the CDC influenza surveillance program, also referred to as FluView, include:

- **Virologic surveillance**—a coordinated effort between the WHO Collaborating Laboratories System and the National Respiratory and Enteric Virus Surveillance System. These efforts include antigenic determination of seasonal influenza viruses, detection of novel influenza A viruses, and genomic surveillance of influenza viruses.
- **Outpatient illness surveillance**—ILINet, a CDC system, captures influenza-like illness (ILI). Outpatient health care providers report weekly patient counts for ILI by age group. The national baseline for ILI is 2.5%, though regional baselines are provided by CDC for each Department of Health and Human Services (DHHS) response region.
- **Long-term care facilities**—a Centers for Medicare & Medicaid Services (CMS) reporting system established for SARS-CoV-2 has now been expanded to also capture influenza activity.
- **Hospital surveillance**—FluSurvNET, a CDC system, conducts laboratory surveillance for hospitalized patients. DHHS requires CMS and non-CMS hospitals to report detailed SARS-CoV-2 and influenza data.
- **Mortality surveillance**—The National Center for Health Statistics (NCHS) calculates the percentage of all deaths attributed to influenza or pneumonia every week. Because pneumonia is a common secondary infection to influenza, its capture is an accurate measure of seasonal flu severity. Pediatric influenza deaths are reported separately from the NCHS data. Pediatric flu deaths are reportable events in most states.

More detailed descriptions of these surveillance systems are located here: [US Influenza Surveillance: Purpose and Methods](#)

Many of these surveillance efforts rely on voluntary reporting to state or federal systems. As such, they represent a subset of the actual impact of influenza. These data are intended to inform public health decisions and provide situational awareness, give insight to health care professionals regarding what viral activity is present and what to expect in the near future, and provide information to the media and public on how to prevent and control the impact of influenza in the community.

The CDC Influenza Division compiles data from all state and territorial health agencies weekly to produce FluView reports. The reports and accompanying dashboards are published and updated weekly throughout the year: [Weekly US Influenza Surveillance Report](#). Summaries of overall activity and data from each FluView reporting system are included in these weekly reports.

The CDC Influenza Division has an emergency contact line that is staffed 24/7.

CDC INFO: [Contact CDC-INFO](#); 800-CDC-INFO (800-232-4636), TTY: 888-232-6348

CDC Influenza Division: 404-639-3747

Additional contact information is in [Appendix B](#).

All states publish custom influenza reports on a weekly basis, typically on state health, public health, or health and human services websites. Most states provide reports from October through March, in alignment with the usual influenza season. State-specific influenza and other respiratory pathogen surveillance reports may be found at the bottom of this site: [Weekly US Influenza Surveillance Report](#).

Impact of SARS-CoV-2 on Influenza Surveillance

Influenza surveillance systems still operate as they did before the SARS-CoV-2 pandemic, though with some reinforced efforts around data collection, reporting, and forecasting resulting from the SARS-CoV-2 pandemic. CDC has indicated potential challenges in differentiating influenza from SARS-CoV-2 in surveillance systems. Both are respiratory pathogens with similar clinical presentations, and coinfections with both influenza virus and SARS-CoV-2, the virus that causes COVID-19, are possible.²⁹⁸

Seasonal Influenza Vaccine Recommendations

CDC provides seasonal vaccine recommendations and clinical guidance for each influenza season here: [Seasonal Influenza Vaccination Resources for Health](#)

[Professionals](#). Vaccine effectiveness studies are performed every year, as antigenic shift or drift between vaccine composition selection and the influenza season may result in a mismatch. Those studies are posted here: [CDC Seasonal Flu Vaccine Effectiveness Studies](#). CDC influenza webpages contain a substantial amount of information, ranging from general information on influenza illness and vaccination for the public to research studies and the Advisory Council for Immunization Practice recommendations. Content is updated frequently and is highly relevant.

Surveillance for Novel Influenza A Viruses in Humans

The US influenza surveillance system can capture swine, avian, or other zoonotic influenza infections in humans through routine surveillance systems. Specimens for human infection submitted to state public health or other laboratories can be subtyped to identify novel influenza A virus strains, which then would usually be submitted to CDC for further sequencing. To date, only swine and avian-origin feline zoonotic influenza virus transmission events to humans have occurred in the United States, with the vast majority attributed to swine influenza virus (SIV). Novel virus subtypes in the United States are limited to A(H7) and A(H1) or A(H3) swine influenza variants. Globally, novel virus subtypes may include A(H2), A(H5), A(H7), and A(H9), as well as SIV A(H1) and A(H3).^{11,100} A potential weakness of the US surveillance system is its dependency on health care providers and laboratories to submit specimens for molecular and genetic testing and subtyping. Only a subset of all influenza virus specimens captured by health care providers are submitted for subtyping, and antigenic test results need to be interpreted differently depending on the prevalence of influenza in the community.⁴ However, the system has worked well in finding novel SIV infections in humans in summer months when seasonal influenza is less likely to occur.²³³

Novel influenza A virus infections in people became a nationally notifiable disease in 2007; this includes all human influenza infections different from circulating human seasonal A(H1) and A(H3) viruses. The [case definition](#) for novel influenza A virus infections also includes human infections subtyped as “nonhuman origin” and those not typable using routine laboratory methods.²⁹⁹ Novel influenza A virus strains are detectable using routine laboratory methods, but the determination of their subtype and confirmation of the strain originating from a nonhuman source currently must be done by CDC’s Influenza Division laboratories or a CDC designated lab.⁴ Rapid detection, reporting, and investigation of novel influenza A virus infections in humans are essential to implement effective public health interventions and promote awareness. All cases are investigated using a Novel Influenza A case report form from this CDC website: [CDC A\(H1N1\) Flu|Clinical Data Collection Forms and Templates](#).²⁹⁹ Investigations might also include the capture of clinical human illness associated with novel influenza A virus infection. In the U.S., illness due to novel influenza A viral

infection is similar in clinical presentation to human seasonal influenza. Persons at increased risk for complications of seasonal influenza are also at risk for serious illness or death from novel influenza virus infection. The most significant outbreak of novel influenza virus in the United States occurred in 2012 (outside of A(H1N1)pdm) when 309 human cases of A(H3N2)v (SIV) were identified, including 16 people who were hospitalized and 1 who died.^{246,300,301}

CDC reports all novel influenza A virus infections in its weekly national influenza surveillance report, FluView, located here: [Reports of Human Infections With Variant Viruses](#). Figure 15 also presents an excerpt from the FluView novel influenza A virus in humans report.

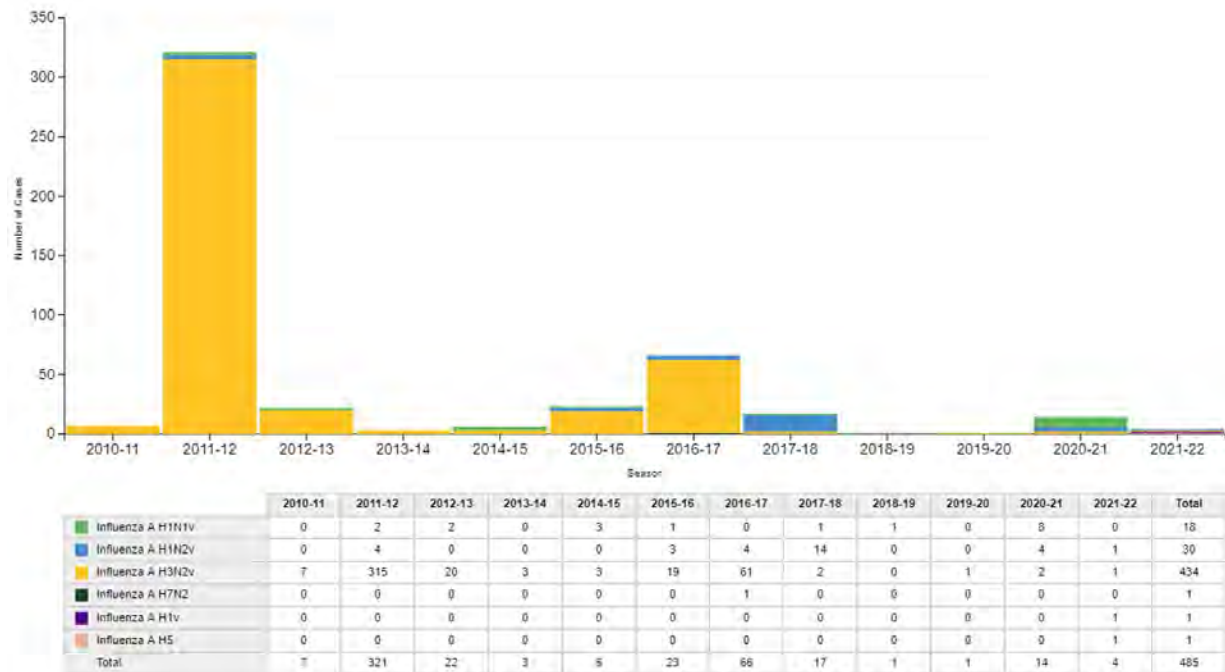


Figure 15. Human novel influenza A virus infections by season and subtype. CDC FluView, 2022.²

International Surveillance of Human Influenza Virus Activity

WHO member countries work collaboratively to monitor influenza viruses in humans. Most of their systems were established to track human seasonal influenza viruses rather than zoonotic infections; however, the systems should also be able to detect novel human infections with influenza viruses that routinely circulate in animals. The WHO Global Influenza Surveillance and Response System (GISRS) was established in 1952, linking 138 National Influenza Centres, 6 WHO Collaborating Centres, 4 Essential Regulatory Laboratories, and several others.⁹²

Laboratory surveillance data are available in real-time on FluNet:

<https://apps.who.int/flumart/Default?ReportNo=2> and

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<https://apps.who.int/flumart/Default?ReportNo=6>. These reports include A(H1) and A(H5) human cases. Additional charts are available here: [Flunet \(who.int\)](#).

Summaries and details of human cases of avian influenza virus (AIV) and swine influenza virus (SIV) are provided semimonthly in the monthly human-animal interface reports: [Global Influenza Programme \(who.int\)](#).

The Weekly Epidemiological Record provides rapid epidemiologic information on infectious cases of new or emerging pathogens and outbreaks, epidemics, or pandemics. While not specific to influenza, this publication contains influenza outbreak notifications: [The Weekly Epidemiological Record \(WER\) \(who.int\)](#).

Novel influenza A virus infections in people are also tracked globally with data coordinated by WHO. In 2005, International Health Regulations (IHR) were formed as a treaty to require reporting and sharing of information regarding public health emergencies of international concern. All member countries must adhere to these reporting rules, and the United States formally accepted this change in 2006. The regulations require that all countries have the ability to detect, assess, report, and respond to public health events encompassed by IHR. The WHO site on IHR is located here: [International health regulations \(who.int\)](#). For more information on the role of CDC in supporting and evaluating IHR and WHO, visit: [International Health Regulations \(IHR\)|Division of Global Health Protection](#).

The WHO IHR site contains disease outbreak news briefs that alert public health officials of emergency events throughout the world: [Disease Outbreak News \(who.int\)](#).

It is important to note that only one-third of member countries have met the requirements of the 2005 IHR treaty.³⁰² While surveillance is becoming increasingly robust, numerous gaps exist in countries with inadequate public health surveillance systems.

The Influenza Research Database is an excellent resource for those seeking detailed genetic or analytic resources for influenza. This site also displays the location, type, and species last infected with a particular strain of influenza virus and contains global information.

[Influenza Research Database–Influenza genome database with visualization and analysis tools](#)

Surveillance of Other Respiratory Pathogens in Humans

Influenza viruses are among many types of viruses that cause respiratory infection; these viruses often intermix throughout colder months in temperate climate countries. In the US, respiratory syncytial virus (RSV) causes significant respiratory disease in infants and young children, potentially resulting in hospitalization and death.

Coinfections of RSV with influenza can occur with severe and potentially lethal outcomes, especially in infants.³⁰³

In the United States, surveillance of non-influenza respiratory pathogens can provide insight into the potential severity of an influenza season, as high rates of these diseases often precede a severe influenza season.³⁰⁴ In addition, the substantial transmission of non-influenza pathogens increases the risk of coinfections throughout the winter months. Pathogens of interest include seasonal coronavirus (non-SARS-CoV-2), human metapneumovirus, human parainfluenza virus, adenovirus, and RSV.³⁰⁴ Codetection of these pathogens with the A(H1N1)pdm09 virus in humans occurred in 2009; codetection also occurred with SARS-CoV-2 infection.³⁰⁵⁻³⁰⁷

Surveillance of influenza and other respiratory pathogens often occurs at the state health agency level with reporting to the National Respiratory and Enteric Virus Surveillance System (NREVSS). While state public health laboratories supply laboratory data to NREVSS, more detailed case data are supplied by state public health agencies to the CDC Influenza Division, usually starting the first week of October and extending through the end of April.

Human Non-influenza Respiratory Pathogen–Specific Surveillance

The following are CDC sources for additional information at the national and regional levels for select non-influenza respiratory pathogens:

- [National Respiratory and Enteric Virus Surveillance System](#)
- Coronavirus (seasonal)–[Coronavirus National Trends–NREVSS|CDC](#)
- Human metapneumovirus–[Human Metapneumovirus National Trends–NREVSS|CDC](#)
- Human parainfluenza virus–[Human Parainfluenza National Trends–NREVSS|CDC](#)
- Respiratory syncytial virus–[RSV National Trends–NREVSS|CDC](#)
- Respiratory adenovirus–[Respiratory Adenovirus National Trends–NREVSS|CDC](#)
- [Unexplained Respiratory Outbreaks \(URDO\)|CDC](#)
- [CDC COVID Data Tracker](#)

Epidemiology and Transmission Dynamics

Seasonal influenza

Seasonal influenza affects populations in the Southern Hemisphere primarily during the US summer months, then moves to the Northern Hemisphere during the US winter months.³⁰⁸ Influenza activity usually begins to increase in late October and extends through March of the following year. In most seasons, either an A(H1) or A(H3) strain will cause the majority of infections. Following the 1977 epidemic of A(H1N1) in Russia

([see previous section–1977–A\(H1N1\)](#)), A(H1N1) began circulating with A(H3N2).⁸⁸ After the pandemic in 2009, A(H1N1)pdm09 now circulates as the predominant A(H1) strain along with A(H3N2). The B/Yamagata strain now circulates much less than B/Victoria and may die out in future seasons.⁹

Other respiratory pathogens and coinfection with influenza viruses

The pandemic caused by SARS-CoV-2 dramatically impacted seasonal influenza patterns in 2020-2021 in all parts of the world.³⁰⁹ In 2020, international influenza activity was negligible, likely because of widespread use of personal protective measures (such as masking and distancing), the absence of large populations of children in school, travel restrictions, and other mitigation efforts used to combat SARS-CoV-2.³⁰⁹ Influenza activity levels for 2021-2022 in comparison to past years are still being assessed.³¹⁰ As SARS-CoV-2 is a significant pandemic in terms of the causal agent, scale, and duration, the long-term impacts of the pandemic on seasonal influenza patterns remain to be seen.

Information on past flu seasons including dominant strains, vaccination, and so forth is located here: [Past Flu Seasons](#).

Influenza Forecasting

CDC provides forecasts of influenza activity updated weekly through the Epidemic Prediction Initiative (EPI). Forecasts are published on [FluSight](#), the CDC flu forecasting website. Researchers external to CDC along with the CDC Influenza Division have worked since 2013 to provide multiple forecasts with differing inputs and algorithms. Forecasts are provided for the entire United States and individual states for case counts and hospitalizations.³¹¹

National FluSight, state, and other forecasts are located here: [Epidemic Prediction Initiative \(cdc.gov\)](#) (*note: forecasting for seasons beyond 2019-2020 may not be available owing to the SARS-CoV-2 pandemic*).

Prevention and Control

Vaccination

Human (seasonal) influenza vaccination is the most effective way to prevent influenza illness. The seasonal vaccine for 2021-2022 in the United States contains 4 influenza virus strains: A(H3N2), A(H1N1)pdm09, B/Victoria, and B/Yamagata. The strain composition of the vaccine is reviewed and adjusted every year based on which strains are circulating and how well the previous year's vaccine protected against influenza.⁶¹

More than 144 influenza centers from 114 countries conduct year-round surveillance for influenza viruses by submitting specimens to the WHO Collaborating Centres.^{61,102} Twice annually, the directors of the collaborating centers along with other

laboratorians meet to assess surveillance, laboratory, and clinical study data to form recommendations for influenza vaccine formulation. A February meeting finalizes recommendations for the Northern Hemisphere vaccine, and a September meeting firms recommendations for the Southern Hemisphere vaccine. Every country decides whether to accept or adjust the WHO recommendations; the US Food and Drug Administration determines the final influenza vaccine composition for the United States.⁶¹

A CDC collection of literature regarding the benefits of influenza vaccination is located here: [Benefits of Influenza Vaccination: Selected Publications](#).

Other prevention and control measures

While vaccination is the most effective way to reduce the spread of influenza, there are many other impactful approaches to prevention and control. Basic respiratory illness prevention measures, all of which were used during the SARS-CoV-2 pandemic, are effective in reducing the spread of influenza. Practices such as handwashing, frequent cleaning and disinfection of high-touch surfaces, covering coughs, use of face masks, isolating when ill, and quarantining when exposed lower the risk of acquiring influenza.³¹² Most people with influenza illness are contagious 1 day before the onset of illness through 3-4 days after illness onset.³¹³

Antiviral treatment may decrease the period of illness and lessen the impact of symptoms if started quickly after the onset of illness. Persons at increased risk for serious illness from influenza are recommended to receive rapid antiviral administration.⁶³

More information from CDC on antiviral medication is located here: [Treatment: What You Need to Know](#)

Avian Influenza Virus (AIV) Surveillance and Epidemiology

International Surveillance of AIV

All highly pathogenic avian influenza (HPAI) infections of any subtype are reportable to the World Organisation for Animal Health (OIE), the animal health equivalent to the World Health Organization, and the agency that maintains the World Animal Health Information System, which is responsible for tracking such infections.^{122,186} Low pathogenicity avian influenza (LPAI) infections are only reportable to OIE by countries that do not have endemic levels of A(H5) or A(H7) activity.¹²² Recent reports of outbreaks of reportable animal diseases are published on the OIE World Animal Health Information System dashboard: [OIE-WAHIS](#).

This interactive dashboard allows search filters for multiple categories: [OIE-WAHIS](#)

Additional collaborative surveillance efforts among wild birds occur through the US Geological Survey (USGS) National Wildlife Center, National Institutes of Health

Centers of Excellence for Influenza Research and Surveillance, the University of Iceland, and others.³¹⁴

Additional AIV Resources: [Avian Flu–FAO’s Animal Production and Health Division](#)

US Surveillance of AIV in Domestic Poultry

The global poultry industry is valued at \$310.7 billion, with an estimated growth rate of 3.8%. Asia has the highest number of chickens in the world, but the Americas produce the most poultry meat as the largest producer and exporter of broiler chickens and turkeys.^{24,315} Outbreaks of LPAI and HPAI often result in mass culling of affected flocks and significant economic impacts to producers and to taxpayers in the form of loss compensation to producers when reimbursed by the government, or loss of international trade business because of the hesitancy of other countries to import potentially infected products.²⁴ The US Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) restricts live poultry imports from countries or regions within countries experiencing HPAI outbreaks affecting commercial or backyard poultry. If the United States experienced sustained HPAI activity, its poultry industry could be dramatically affected.³¹⁶

Domestic surveillance and requirements for testing of bird flocks vary by state. All states have a National Poultry Improvement Plan (NPIP) with participating facilities listed here: [NPIP Participants States \(poultryimprovement.org\)](#). NPIP coordinators and testing programs are funded through a cooperative agreement with USDA.³¹⁷ Information about state coordinators for testing is in a centralized document located here: [OfficialStateAgencies.pdf](#).

NPIP state coordinators solicit avian serum collection for each flock at least annually, though frequency depends on the growing/production period of a flock and the capacity of the producer. Testing is typically inclusive of serology for evidence of recent or past infection and PCR for acute infection with AIV. Samples may also be tested by the USDA, and all specimens with AIV presumptive positivity are verified and subtyped by USDA State Animal Health Officials (SAHOs), who may require testing at agricultural fairs, markets, or other situations, including those in which morbidity or mortality within a flock is evident. Commercial producers submit for testing regularly; required testing of backyard flocks, free-range flocks, and other production types may be enforced by NPIP coordinators or SAHOs.³¹⁷

Requirements for interstate movement of birds or eggs are determined by the SAHOs in the state of destination. These requirements often include testing of the flock of origin for NPIP certification on a 9-3 movement form or a certificate of veterinary inspection. States may also have premovement avian influenza testing requirements, and some states may require “AI clean” certification.³¹⁷

USDA APHIS routinely posts US HPAI outbreak information here: [Highly Pathogenic Avian Influenza \(HPAI\)](#)

Surveillance of AIV in Wild Birds

US surveillance of AIV

The US National Surveillance Plan for Highly Pathogenic Avian Influenza in Wild Birds was implemented in 2015 to maximize US ability to detect AIV in wild waterfowl. Surveillance helps to (1) understand how IAV is distributed in the United States, (2) detect the spread of IAV to new areas of concern, (3) monitor wild dabbling duck populations for introductions of novel viruses, and (4) estimate the apparent prevalence of IAVs of concern (e.g., Eurasian lineages A(H5) and A(H7)). This plan includes collaborative surveillance efforts conducted by several federal agencies, including USDA APHIS, the US Department of the Interior's (DOI) USGS and Fish and Wildlife Service (FWS), as well as state departments of natural resources.^{13,318,319}

Surveillance of AIV in wild birds is specifically targeted to:

- Investigating morbidity and mortality events (e.g., within parks and refuges)
- Sampling live wild birds
- Sampling in hunter-harvested birds
- Sentinel species placement (e.g., placement of sentinel ducks on backyard premises or within bird colonies)
- Environmental sampling of fecal material

This document from USDA APHIS details sampling approaches and responses to wild bird AIV events:

https://www.aphis.usda.gov/animal_health/downloads/animal_diseases/ai/wild-bird-strategic-plan.pdf.

This document outlines the national approach to AIV surveillance in wild birds: [US Department of Agriculture \(usda.gov\)](#).

The USGS FWS supports surveillance efforts for HPAI in wild birds: [Avian Influenza Surveillance](#).

Most of the concern since 2000 has been A(H5) viruses, but A(H7) in wild birds is growing in prevalence. Although a small percentage change, A(H7) was identified in < 1% of bird specimens in 2020 and increased to > 1% in 2021. More than 3,700 cases of HPAI were detected in domestic and wild birds in Europe in 2020-2021. APHIS is working to create a public-facing dashboard for AIV slated for release in 2022.³²⁰

Multiple US government and international agencies publish surveillance reports for AIV in domestic and wild (terrestrial and aquatic) birds. Table 3 provides links to these reports.

Table 3. Domestic and wild bird avian influenza virus surveillance information and reports—US and international

	United States	International
Avian (domestic)	WHISPers (usgs.gov) USDA APHIS avian influenza and wild birds	Avian influenza—OIE—World Organisation for Animal Health OIE-World Animal Health Information System (WAHIS)
Avian (wild—terrestrial and aquatic)	WHISPers (usgs.gov) Avian influenza US Geological Survey (usgs.gov) Avian influenza and wild birds	

The following is a list of all State Animal Health officials in the United States and its territories: [Federal and State Animal Health \(usaha.org\)](#).

National Animal Health Laboratory Network (NAHLN) laboratories are listed at [www.aphis.usda.gov/animal_health/nahln/downloads/ai_lab_list.pdf](#). The listed laboratories are those that can currently perform testing for avian influenza viruses. During an outbreak, the National Veterinary Services Laboratories must confirm HPAI viruses.³¹⁸

A multidecade review of AIV frequency involving surveillance of North American waterfowl in Canada and the United States found that peak activity occurred in late summer, declined in fall and winter, then increased in spring. Higher prevalence was found among females and in juvenile birds.^{321,322} Longitudinal surveillance infers trends of increasing hemagglutinin (HA) subtype diversity and decreasing AIV prevalence throughout a migration season.³²¹

Ecology of US and International Flyways and AIVs

Migratory flyways

As migratory birds have the potential to carry AIV, their migratory flight patterns can be examined to determine which strains of AIV are being carried where and by what bird species, as well as the potential risks these birds pose regarding the introduction of AIV to domestic birds. North American flyways are routes within larger, defined international flyways. There are 4 major flyways in the US: the Pacific, Central, Mississippi, and Atlantic (Figure 16). Most migratory bird species use a single flyway to migrate during spring and fall, though some species cross multiple flyways. Detections of American lineage A(H7) AIV have occurred in summer, fall, and winter, and usually

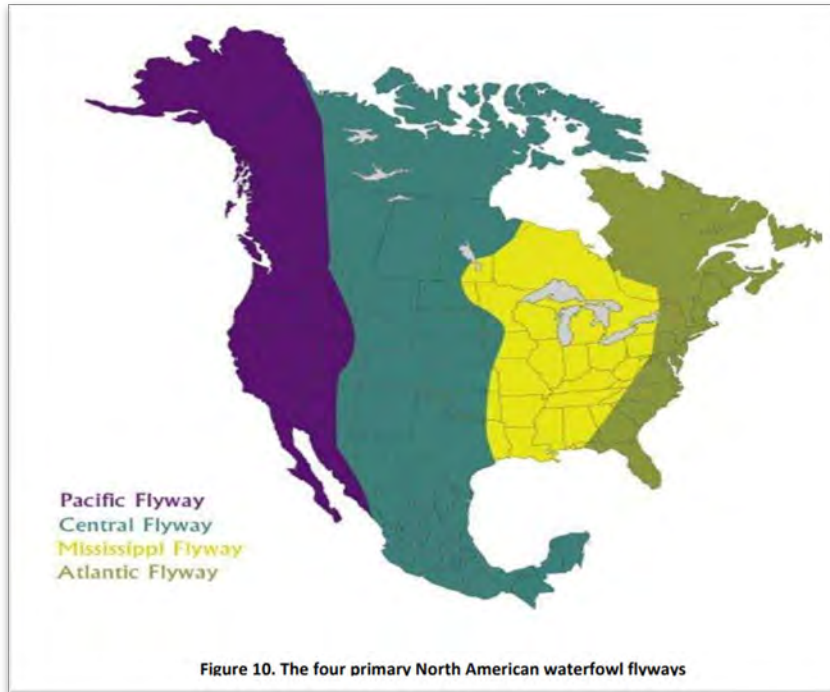


Figure 16. North American waterfowl migratory flyways. USDA APHIS, 2017³

peak in early winter.¹⁹¹ Eurasian lineage A(H5) AIV were first introduced to North America, resulting in a large HPAI outbreak from birds that migrated from Asia to North America in 2014.¹⁴⁹

Widely recognized international flyways include the Pacific Americas, Atlantic, East Atlantic, Black Sea/Mediterranean, East Africa and West Asia, Central Asian, Asian-Australian, and West Pacific (also referred to as the Pacific or Alaska flyway) (Figure 17).^{314,323,324} These

flyways span the length of the world from north to south and across numerous continental latitudes.

Introduction of Eurasian strains of AIV is believed to occur through overlap in the northern terminus of the North American and Eurasian flyways. Within North America, Eurasian A(H5) AIV have been detected in wild birds in the Atlantic and Mississippi flyways.⁸⁴

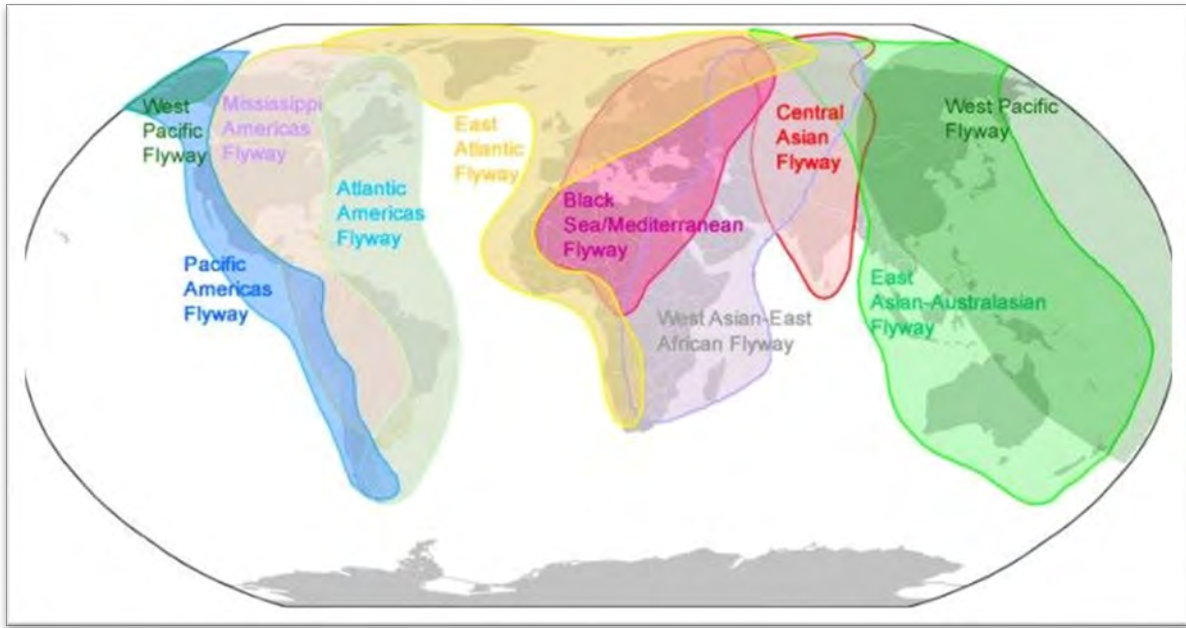


Figure 17. International bird migration flyways. *Migratory Birds Without Boundaries*, 2022.³²⁴

Frequent recurrence of HPAI in wild and domestic birds in Europe since 2006 resulted in increased coordination of surveillance in the North Atlantic.¹³ Other significant factors contributing to the need for heightened surveillance in this region were raised by the USGS in 2018, including:

- Genetic evidence of frequent mixing of North American and Eurasian lineages
- Genetic similarities between Icelandic influenza viruses and those causing seal mortality in Europe
- Genetic relationships to HPAI A(H5N1) among viruses detected in Iceland, the United States, and other European countries.¹³

Epidemiology and Recent Outbreaks—US

Wild aquatic birds, particularly dabbling ducks, serve as the natural reservoir for LPAI viruses globally and in the US. LPAI serves as a precursor to HPAI in domestic birds, though wild birds can also carry HPAI. Before a 2015 multistate outbreak of HPAI in the US, genetic analyses showed that an interaction between migratory birds of Asia and Alaska resulted in a reassortment event in which an Asian HPAI strain mixed with a North American LPAI virus.¹⁴⁹ Therefore, ducks and other wild birds migrating through and across the Pacific, Central, Mississippi, and Atlantic flyways pose a significant exposure risk for domestic birds.

HPAI/LPAI A(H5N1) Outbreaks in the U.S. - multiple states - 2022

The first outbreak of 2022 in domestic poultry in the U.S. was detected in turkeys in Indiana in February. Multiple outbreaks rapidly followed with the majority of U.S. states

(34) reporting outbreaks (Figure 19). As of May 9, 2022, 37.55 million birds have been affected among 172 commercial flocks and 120 backyard flocks (Figure 18).¹²⁶

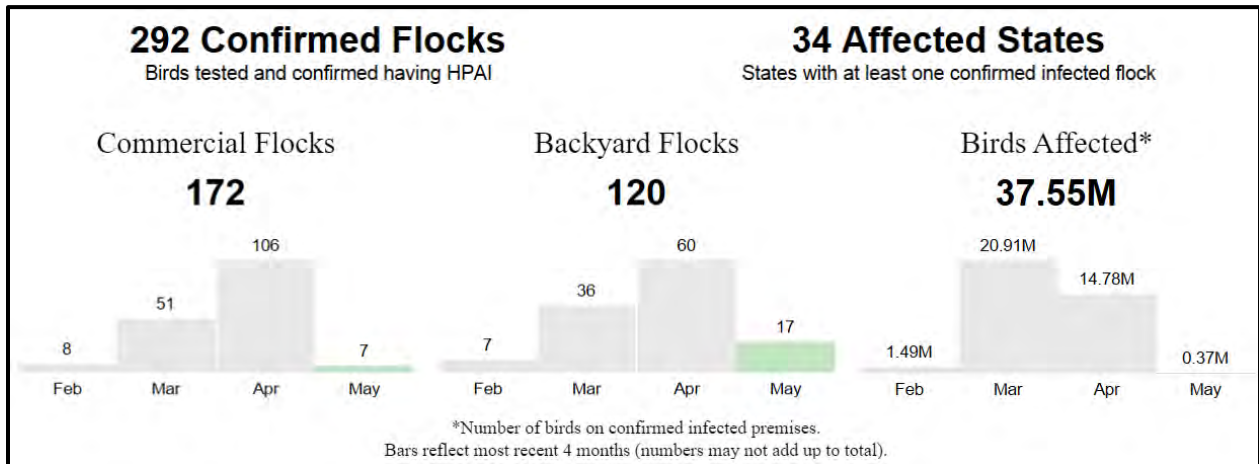


Figure 18. HPAI H5 detections in the U.S., Jan-May 2022, USDA APHIS³²⁵

The heaviest concentration of cases is in Iowa where over 13 million birds have been culled from 15 commercial flocks and 4 backyard flocks.¹²⁶

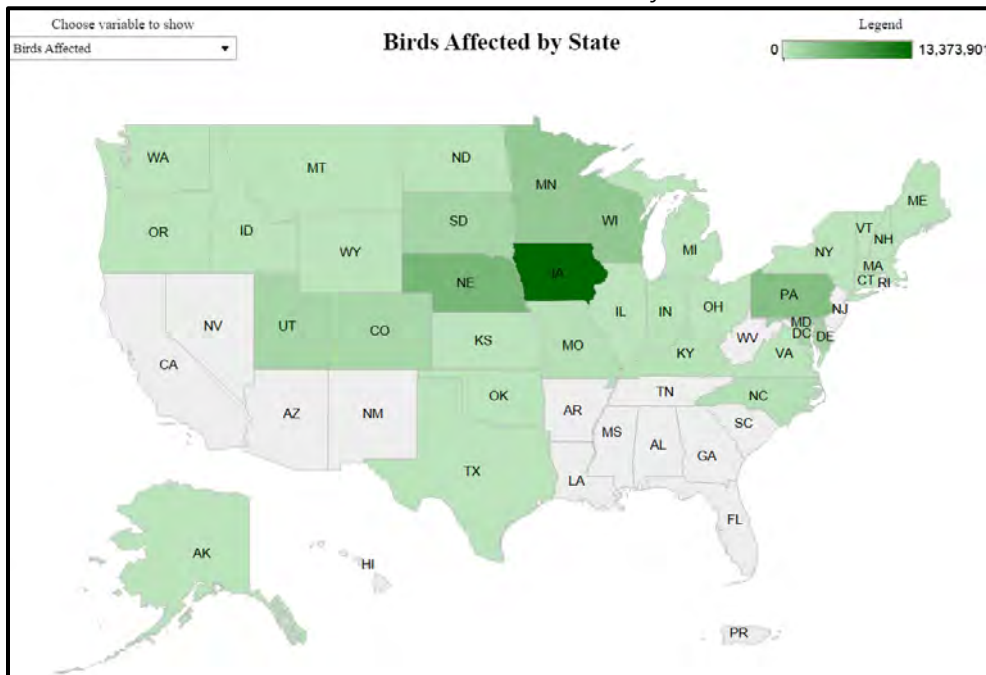


Figure 19. Birds affected by HPAI H5 by state, USDA APHIS, 2022¹²⁶

Prior to the current outbreak, an exceptional number of HPAI detected were identified in wild birds with only 12 states not reporting positive cases (Figure 20). The earliest cases were found in birds in South Carolina and North Carolina. While early wild bird cases were the Eurasian/North American reassortant strain, the dominant influenza virus is the Eurasian H5 2.3.4.4b, which is highly pathogenic to poultry.¹²⁷

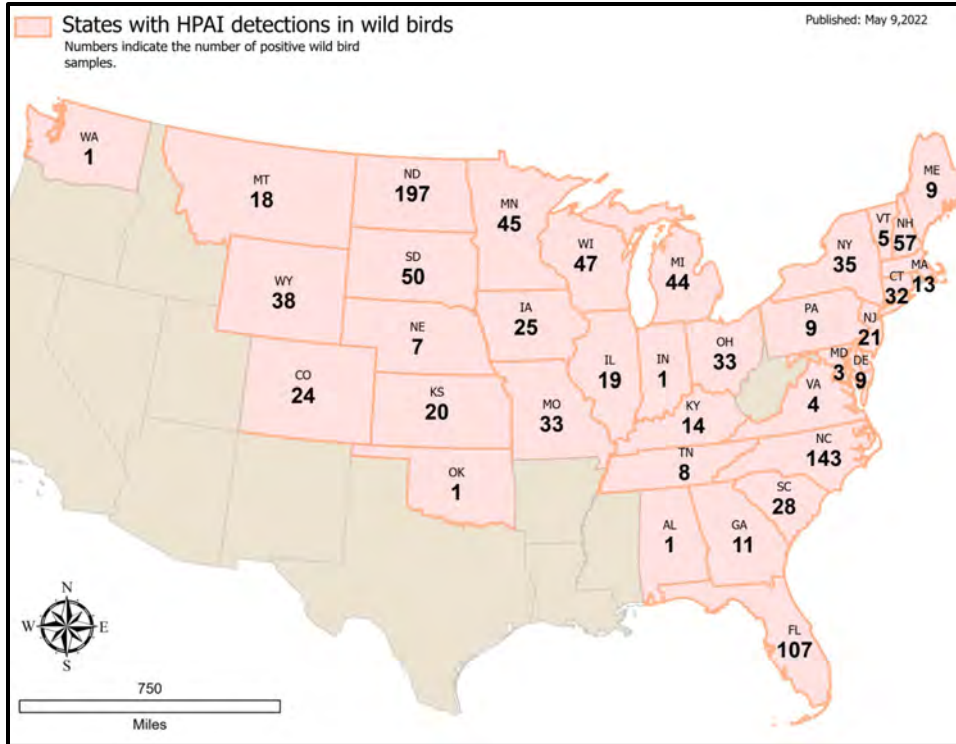
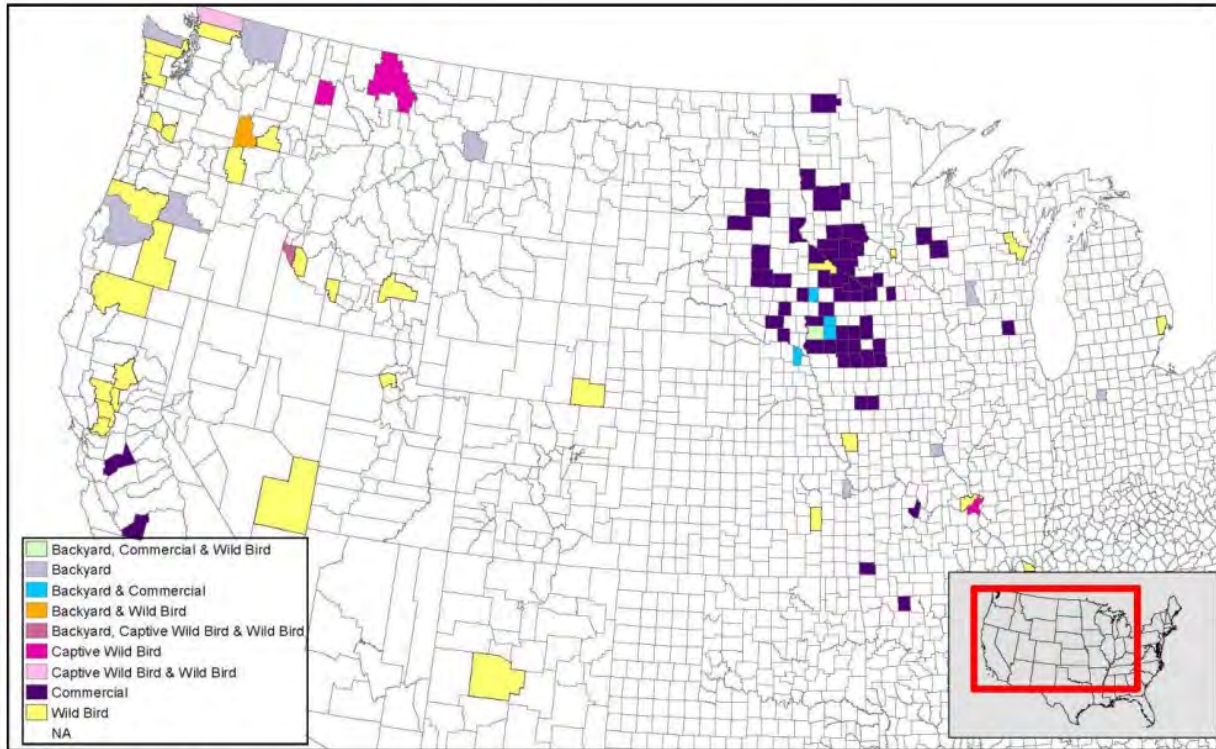


Figure 20. Wild birds affected by HPAI H5, USDA APHIS 2022¹²⁷

HPAI A(H5N2)/A(H5N8)/A(H5N1) Outbreaks in the U.S. - multiple states–2014-2015

In the 2014-2015 HPAI outbreak in the United States, A(H5N2) was the most common subtype of HPAI, followed by A(H5N8) and A(H5N1).¹⁶ The outbreak affected commercial and backyard poultry flocks and captive or wild birds in 21 states and resulted in the depopulation of 7.5 million turkeys and 42.1 million chickens (Figure 21).³²⁶

The 2014-2015 HPAI outbreak is the largest ever in the United States and resulted in the loss of 50.5 million commercial birds (depopulated or succumbed to the virus) mostly infected with A(H5N2). The first case was detected in December of 2014, and the last case was confirmed on June 16, 2015. Based on the calculations made in June/July 2015, the death/depopulation losses represent 7.46 percent of average U.S. turkey inventory, 10.01 percent of the average layer inventory, and 6.33 percent of average US pullet inventory. Broilers were mainly unaffected during the outbreak. The economic impact was an estimated \$3.3 billion.⁹⁶



Note: Map produced during the incident by USDA APHIS VS Center for Epidemiology and Animal Health, showing all detections December 2014 to June 2015.

Figure 21. Highly pathogenic avian influenza virus infections in all birds as of August 31, 2015, United States. USDA APHIS, 2016¹⁵⁸

HPAI H7N8 Indiana–2016

The presence of HPAI A(H7N8) in a commercial turkey flock was confirmed in January 2016. The virus was of the North American lineage with high similarity to wild bird strains circulating at the time. The outbreak affected 10 farms that shared company and feed trucks within 14 days of infection.²¹⁹

LPAI and HPAI A(H7N9) Tennessee and multiple states–2017

In March 2017, HPAI A(H7N9) was detected in a commercial broiler chicken breeder farm in Tennessee (Figure 22). Testing confirmed the strain was of the North American lineage and not related to the Asian A(H7N9) HPAI virus. Lateral spread to multiple complexes occurred, and additional farms were identified with broilers infected with HPAI A(H7N9). LPAI was also detected in this outbreak and was potentially cocirculating with HPAI. The outbreak rapidly spread to other farms with different production types and in additional states (Figure 22).¹⁵⁸

State	County	Production Type	Pathogenicity	Confirmation Date
Tennessee	Lincoln	Commercial Broiler Breeder	HPAI	3/4/2017
Tennessee	Giles	Commercial Broiler Breeder	LPAI	3/8/2017
Alabama	Madison	Backyard Producer	LPAI	3/10/2017
Alabama	Lauderdale	Commercial Broiler Breeder	LPAI	3/14/2017
Alabama	Jackson	Backyard Producer Guinea Fowl	LPAI	3/15/2017
Tennessee	Lincoln	Commercial Broiler Breeder	HPAI	3/15/2017
Tennessee	Lincoln	Backyard Producer	LPAI	3/15/2017
Tennessee	Lincoln	Backyard Producer	LPAI	3/15/2017
Alabama	Pickens	Commercial Broiler Breeder	LPAI	3/16/2017
Alabama	Madison	Backyard Producer	LPAI	3/17/2017
Kentucky	Christian	Commercial Broiler Breeder	LPAI	3/17/2017
Alabama	Cullman	Commercial Broiler Breeder	LPAI	3/21/2017
Kentucky	Christian	Backyard Producer	LPAI	3/21/2017
Georgia	Chattooga	Commercial Broiler Breeder	LPAI	3/25/2017

Figure 22. Location, type, pathogenicity, and date of infected flocks during the A(H7N9) highly pathogenic avian influenza/low pathogenicity avian influenza virus outbreak.³

A(H7N3) (LPAI & HPAI) North and South Carolina–2020

LPAI and HPAI A(H7N3) were detected in North and South Carolina in March 2020 in domestic turkeys. Analysis suggests the virus emerged from wild waterfowl from the Mississippi flyway, resulting in an outbreak of LPAI in several barns and HPAI in 1 barn in North Carolina and 1 barn in South Carolina. No birds were sent to slaughter before testing and detection of AIV, thus limiting potential exposure in production processing.³²⁷

Infections of AIV in Humans–International 2021 and Beyond

Prior to 2016, bird infections with AIV A(H7N9) and A(H5N1) were very high in Asia, with limited reports since then. However, from 2020 to the present, the number of outbreaks observed in birds globally, especially in Europe and Africa, has been much higher than that in the previous 20 years.¹⁸⁶ Northern Ireland reported its largest-ever outbreak at the end of 2021.³²⁸

The tracking of AIV infections in humans is coordinated by WHO, though epidemiologic details of each case report depend on what member countries are able to provide. WHO provides quasi-monthly reports of AIV human infections with risk assessments by strain titled "[Influenza at the animal-human interface summary and](#)

[assessment](#).¹⁰² The country of residence for each case is not always available. These reports also include human cases of swine (or variant) influenza virus infections.

WHO reports on novel human AIV and SIV infections are located here: [Global Influenza Programme \(who.int\)](#)

WHO also tracks cumulative counts of AIV A(H5N1) infections in humans here: [Global Influenza Programme \(who.int\)](#)

Human Cases of Avian Influenza A(H5N6), A(H5N8), A(H9N2), and A(H10N3)–international–2021

As of January 8, 2022, there were a total of 66 AIV cases reported globally in humans for all of 2021 (Table 4). Two strains were dominant in 2021: A(H5N6) and A(H9N2). For most cases in which epidemiologic details are available, all cases were confirmed to have direct or indirect contact with infected birds or contact with a virus-contaminated environment, whether in backyard farms, through exposure at work, or at a live animal market prior to the onset of illness.³²⁹

Table 4. Human cases of avian influenza virus by subtype in 2021³³⁰

	H5N6	H9N2	H5N8	H10N3	H5	Total
Case count^a	30	21	7	1	7	66

^aCase counts may be updated in future reports from the World Health Organization.

At the start of 2021, only 29 laboratory-confirmed human infections with A(H5N6) had been reported since 2016.¹¹⁷ In 2021, 30 cases were reported, 12 of which were confirmed from China. An unusually high number of A(H9N2) cases were reported in 2021, with 21 total and 15 of 21 confirmed in China. China also reported 1 case of A(H10N3).^{128,329,331}

Russia reported several infections with A(H5N8) in humans, along with substantial domestic and wild bird outbreaks along the southwest border with Kazakhstan.¹¹⁷

Nigeria reported 7 human cases of A(H5); specimens could not be subtyped by WHO but were believed to be related to avian outbreaks occurring at the time of human infection.¹¹⁷

India also reported 2 cases of A(H5) in teenagers with distant exposure to birds.³³¹

Human cases of Avian Influenza A(H5N6), A(H5N8), A(H9N2), and A(H10N3)–international–2022

Between January 22 through April 7, 2022, the WHO reported 19 cases of AIV in humans. Cases were from China and Cambodia.^{329,332}

Table 5. Human cases of avian influenza virus by subtype in 2022

	H5N6	H9N2	Total
Case count	11	8	19

The First U.S. Human Case of Avian Influenza

The first case of AIV in a person in the U.S. was reported on April 28, 2022. The person resided in Colorado and had extensive contact with sick poultry through participation in the culling process.^{243,333} The patient was treated and recovered. This is the second case of A(H5N1) of the clade 2.3.4.4b, with the first case having been reported in the United Kingdom in December 2021. The A(H5N1) clade 2.3.4.4b virus is the most common strain circulating among birds internationally.²⁴³ For more information on how this outbreak is affecting birds, [see this section](#).

This U.S. case coincides with a substantial outbreak of HPAI ongoing in the domestic poultry population.³²⁵ For more information on this case, the strain, and the current situation visit:

[U.S. Case of Human Avian Influenza A\(H5\) Virus Reported | CDC Online Newsroom](#)
[Current U.S. Bird Flu Situation in Humans | Avian Influenza \(Flu\)](#)
[UPDATE: U.S. Case of Human Avian Influenza A\(H5N1\) Virus Reported](#)

Recent International Surges in HPAI and LPAI Outbreaks in Birds

The number of AIV outbreaks in birds was also substantial in 2021, as were the number of countries affected (Figure 23). Multiple countries in Europe, southern Africa, the Middle East, and Asia (including Japan) saw outbreaks of HPAI resulting in mass culling of affected poultry flocks (Figure 24).¹⁸⁶

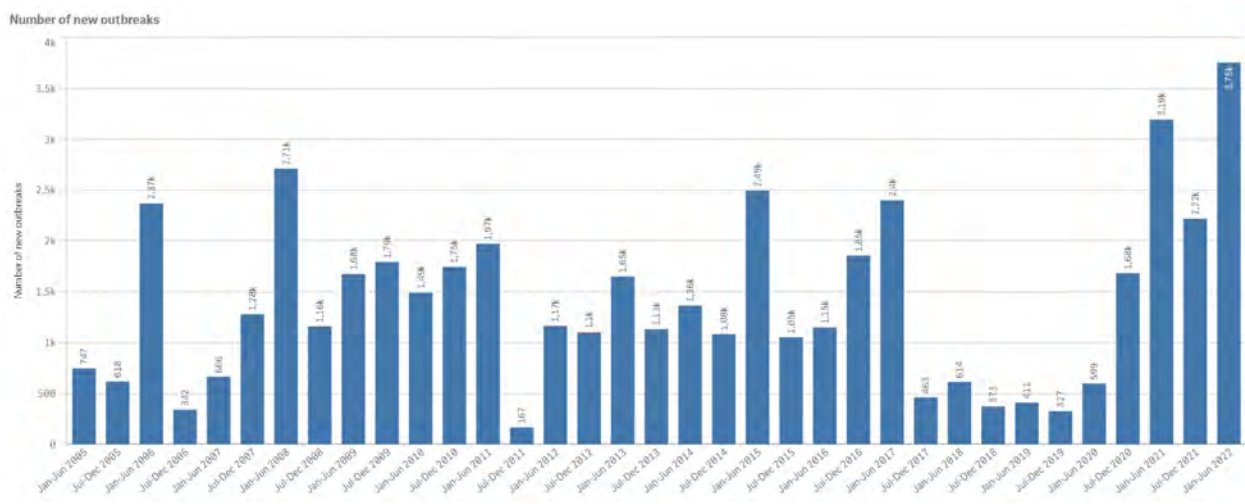


Figure 23. Count of new avian influenza virus outbreaks in birds by month and year.¹

The OIE closely tracks outbreaks of HPAI as a reportable condition in birds. These dashboards are updated frequently and are located here: [OIE-WAHIS](#).

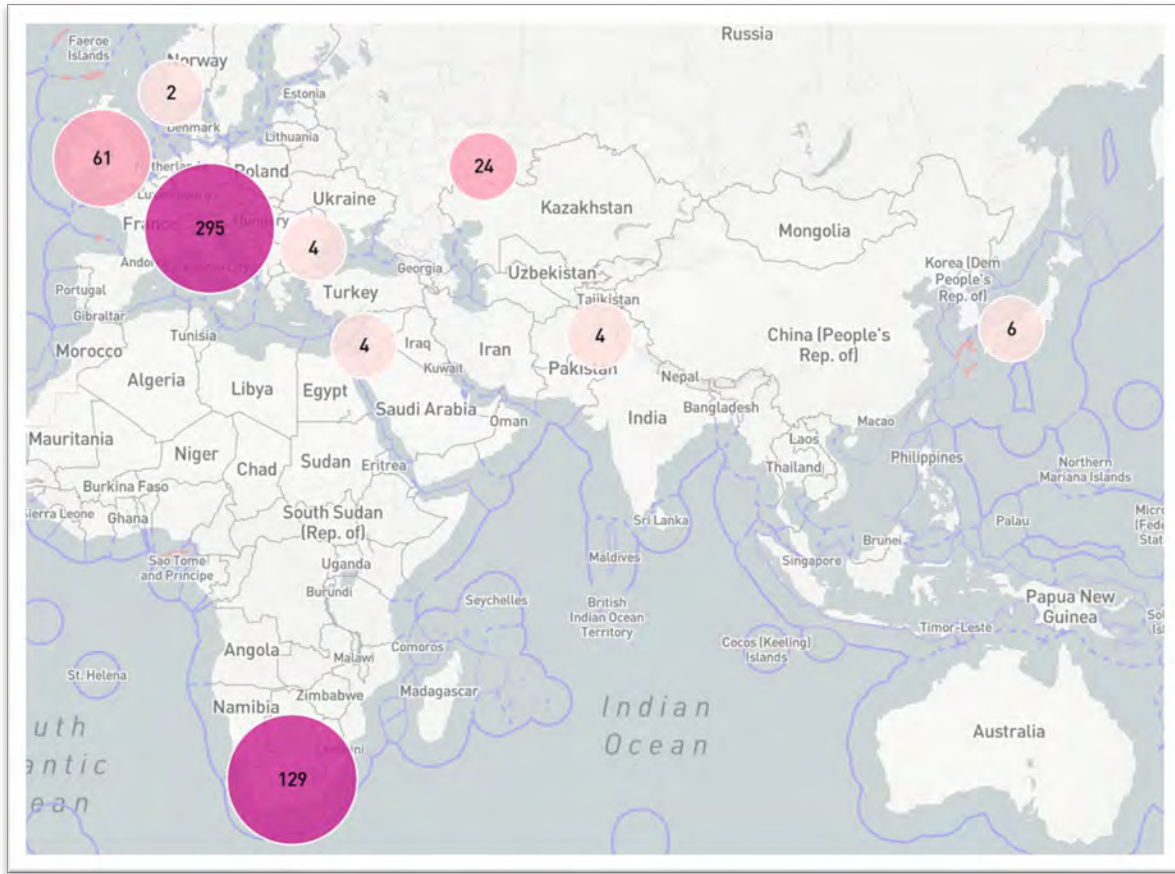


Figure 24. Count of new outbreaks of avian influenza virus by location. OIE WAHIS, 2022. ¹

Prevention and Control of AIV

Transmission among birds and between birds and people

AIV is most commonly spread from birds to other susceptible hosts through the feces of infected birds and secretions from the nose, mouth, and eyes of birds (Figure 25). Susceptible hosts acquire infection when coming into direct contact with infected birds and their secretions or when coming into contact with infected bird feces or water contaminated with infected feces. Domestic flocks raised in open flight pens or on a range might come into contact with feces or water contaminated with feces from infected wild aquatic birds. Within a flock, poultry house transmission might occur via airborne droplets (Figure 25). [326,334,335](#)

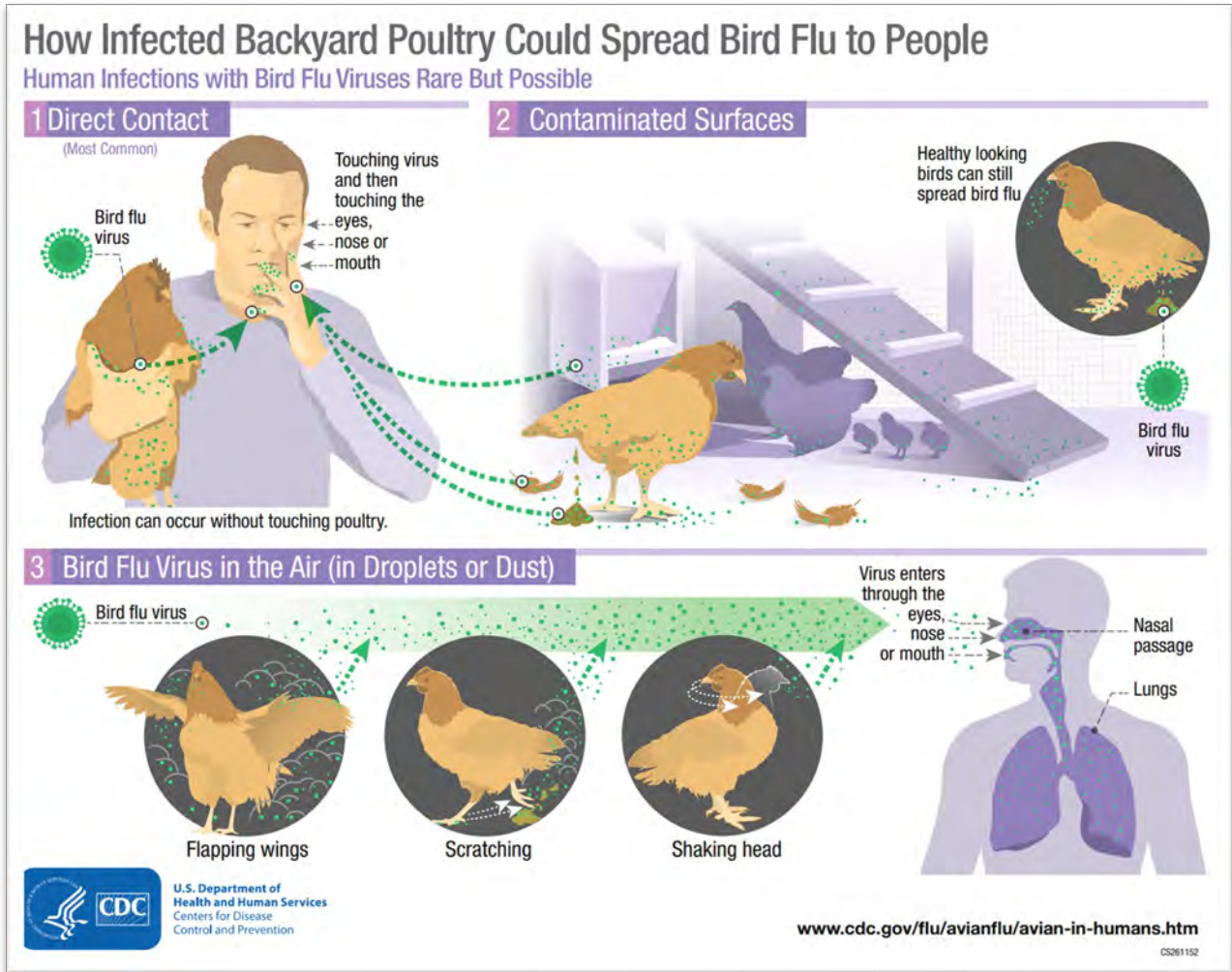


Figure 25. How infected backyard poultry could spread bird flu to people, CDC, 2022.

Epidemiologic investigations have determined that farm-to-farm spread almost always follows movement of contaminated equipment and people. Transmission via infected wild bird from farm to farm is unlikely.^{318,335}

AIV transmission from food

Eggshells can contain AIV on their surface and are therefore a potential vehicle for transmission. Proper handling and cooking of eggs will kill AIV.³³⁵ While consuming undercooked or improperly cooked meat of an infected bird could cause AIV infection in humans or other animals, a human case has never resulted from proper handling or cooking of a bird infected with AIV in the United States.^{137,334} With at least 1 recent case of HPAI(H5N6) in China, infection occurred after a person purchased and consumed a recently slaughtered duck from a local market, suggesting that foodborne transmission is possible.³³⁶

International marketing, production, and biosecurity

The Food and Agriculture Organization of the United Nations (FAO) and OIE have classifications for poultry production systems based on the presence of biosecurity measures.^{24,107} Sector 1 is composed of industrial poultry with high biosecurity. Sector 2 includes large commercial producers under contract with major agricultural companies with good biosecurity. These 2 sectors are primarily in industrialized countries predominating in the international trade of poultry. These countries include the United States, Canada, Australia, Brazil, Malaysia, Thailand, the European Union.^{24,337}

Sector 3 is largely composed of commercial, small to medium producers with low investment in biosecurity. This sector includes diverse producers such as organic, free-range, smaller-scale facilities with quick turnover, ducks raised by grazing on rice paddies, birds raised for cock fighting, and other niche production areas.²⁴ Countries in this sector include Indonesia, Egypt, Turkey, Vietnam, China, and Nigeria.

Sector 4 includes mainly backyard flocks, small urban flocks, and birds raised for household consumption. Most flocks in this category are not recorded in government systems.²⁴

The risk for the emergence of HPAI and other emerging AIV strains is highest among systems with the greatest diversity. While biosecurity in sectors 1 and 2 generally entails extensive, proactive surveillance and detection mechanisms and operational plans for control of AIV outbreaks, sectors 3 and 4 present substantial risks to future avian and human health as they lack the biosecurity measures of sectors 1 and 2.^{24,337}

International market chains involve the exchange of feed, vaccines, carcasses, bird products (e.g., feathers), and live animals; therefore, an outbreak in 1 country can impact several others economically. Even smaller production countries have complex contracts and production cycles involving multiple growers, processors, wholesalers, sellers, and live markets. These interrelationships are challenging to trace during disease outbreaks and the impacts of disease may be far-reaching.²⁴

Production controls and interstate transport

As previously stated, in the United States, NPIP, in cooperation with USDA and state animal health officials, manages poultry flock testing and certification required for interstate transport. Certification status by state is listed on the NPIP site here: [NPIP Participants States \(poultryimprovement.org\)](https://www.npip.org/ParticipantsStates). State NPIP coordinators regularly offer biosecurity training for producers from commercial (sectors 1 or 2) to backyard flock owners.³¹⁷

The NPIP, in conjunction with the USDA, publishes a National Poultry Improvement Plan Program Standards document (last updated December 2019). This plan provides extensive guidance for states drafting or revising their state-level plan. It includes

recommendations for animal testing, bacteriological examination, sanitation, and molecular examination, as well as biosecurity principles. While the document encompasses all major threats to poultry, it includes AIV guidance. The Standards document is located here: [ProgramStandardsA-E.pdf \(poultryimprovement.org\)](#).

Prevention and control

The OIE was formed in 1924 through an international agreement.⁹³ The OIE is responsible for improving animal health and publishes animal-specific terrestrial reference guides. The OIE is recognized by the World Trade Organization and includes a total of 182 member countries with regional and subregional offices on every continent.⁹³

OIE maintains a list of 204 notifiable terrestrial and aquatic animal diseases. Highly pathogenic avian influenza and equine influenza virus infections are included.^{122,186,338,339} Countries with endemic LPAI A(H5) or A(H7) activity may choose to report their status to OIE as well. The entire list is located here: [Animal Diseases–OIE–World Organisation for Animal Health](#). As previously stated, the OIE closely tracks AIV outbreaks on a publicly available dashboard and produces routine reports.¹⁸⁶

Investigation of situations of interest

Agency roles and responsibilities

In the United States, when an outbreak of HPAI or LPAI virus occurs in domestic poultry, the response is coordinated by state animal health officials and by USDA APHIS. The USDA APHIS *Highly Pathogenic Avian Influenza Response Plan: The Red Book* was last updated in 2017 and provides an extensive guide for state and local responses. Contact information for APHIS is in Appendix B. Local public health agencies may have a role in outbreak response during an HPAI or LPAI investigation, because of the risk of potential human infection in workers and responders. Use of appropriate personal protective equipment, surveillance for influenza-like-illness, and testing for influenza in ill workers should be a component of these animal outbreak response activities.³⁴⁰

[HPAI Response Plan: The Red Book \(Updated May 2017\) \(usda.gov\)](#)

Response to infections or outbreaks in wild birds involves coordination between USDA, the Department of the Interior (DOI), Wildlife Services, and the state departments of health, agriculture, and natural resources.

The Red Book also includes information about collaborative surveillance efforts conducted by the USDA APHIS, DOI US Geological Survey and Fish and Wildlife Service, and the state departments of natural resources.³¹⁸

International response

Multiple international organizations work collaboratively using a One Health approach to detect, monitor, report, and respond to international AIV-related emergencies in animals. Leading organizations include the World Organisation for Animal Health (OIE), United Nations Food and Agriculture Organization (FAO), their joint organization referred to as OFFLU, the World Health Organization (WHO), and the United Nations Environment Programme (OIE, FAO, and WHO form the Tripartite). Their response plans and cross-collaboration documents are located as follows:

FAO [Avian Flu—FAO’s Animal Production and Health Division—home](#) and the approaches to controlling, preventing, and eliminating A(H5N1) highly pathogenic avian influenza in endemic countries at <https://www.fao.org/3/i2150e/i2150e.pdf>.

OIE resources include a chapter in the *Terrestrial Animal Health Code* titled “Infection With High Pathogenicity Avian Influenza Viruses”; the objective of the chapter is to “mitigate animal and public health risks posed by infection with high pathogenicity avian influenza viruses. ...”³⁴¹The chapter is located here: [Terrestrial Code Online Access—OIE—World Organisation for Animal Health](#). The OIE *Terrestrial Manual* includes a chapter on avian influenza (including infection with high pathogenicity avian influenza viruses) that provides an extensive overview of the pathogen and its manifestations in birds, the potential to spread beyond its host species, and prevention and control of infections and outbreaks. The manual is located here: [Avian influenza \(oie.int\)](#).

Tripartite+: [Collective Action for our One Health—Food Systems Summit Community](#)

OFFLU: [OFFLU Network on Avian Influenza](#)

WHO: [Avian and other zoonotic influenza \(who.int\)](#)

Tripartite Guide to addressing zoonotic diseases in countries:
<https://www.who.int/initiatives/tripartite-zoonosis-guide>

Swine Influenza Surveillance, Epidemiology, Prevention & Control

Epidemiology

Swine influenza virus (SIV) is common among swine populations. Internationally, 25% of swine show evidence of serologic immunity to cH1N1; serologic evidence is 30% in US herds and > 50% in the North Central United States.³⁴² SIV circulates seasonally at endemic levels but can also emerge as abrupt epidemics that have more significant impacts. Swine herds with endemic influenza may be asymptomatic, even at the height of circulation, which usually follows periods of heat or cold stress. Endemic spread may result in sporadic abortions or low conception rates in addition to apparent clinical illness. Epidemic infection can occur in all age groups of swine, with disease onset typically being acute and dramatic.³⁴³

Surveillance

Surveillance for SIV in the United States is voluntary and conducted by USDA APHIS in cooperation with states and industry. The intent of swine surveillance is to identify influenza strains circulating in swine populations to improve diagnostic tools and animal vaccines, as well as potentially find spillover events in which human seasonal influenza has infected pigs.²²⁷

The USDA National Animal Disease Center in Ames, Iowa, provides quarterly reports of SIV surveillance, including strain subtypes and phylogenetic analyses.

What is Influenza A Virus in Swine (IAV-S)	Swine influenza–OIE–World Organisation for Animal Health
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Influenza surveillance in swine (see the IAV-S Surveillance section): [USDA APHIS|What is Influenza A Virus in Swine \(IAV-S\)](#)

Novel influenza A surveillance in humans (CDC FluView):

https://gis.cdc.gov/grasp/fluview/Novel_Influenza.html

When criteria are met, SIV may be designated as an emerging disease under the [Terrestrial Animal Health Code defined by the World Organisation for Animal Health \(OIE\)](#).³⁴⁴ Human infection with a novel influenza A virus (IAV) originating from swine or other animals is nationally and internationally notifiable given the pandemic potential of any novel IAV infection in humans.^{12,343} Given that influenza is endemic in swine populations, reporting of SIV is not required per OIE.³⁴⁵ The USDA focuses testing efforts on swine populations meeting the following criteria:

- 1) Farms with pigs exhibiting symptoms of influenza-like illness (ILI)
- 2) Swine exhibiting ILI at concentrated gatherings such as auctions, markets, fairs, or exhibition events
- 3) Swine epidemiologically linked to a confirmed case of SIV in a human³⁴³

The [National Plan for Swine Influenza Surveillance](#) is published by USDA APHIS and includes testing strategies and protocols for the epidemiologic investigation of SIV in swine.³⁴³

There is extensive discussion among government agencies regarding the need for expanded surveillance of SIV. The swine industry is critical to the US food supply and domestic employment, as well as being the origin of substantial exports.³⁴³ The risks of not increasing the scale and scope of surveillance include:

- Potential pandemic human illness;
- Severe illness and death in pig populations;
- Increased risk among farmworkers and their families for transmitting influenza infection to or from the pigs for which they care
- Reduction in caretaker attendance and animal care compliance in the wake of the threat of an influenza pandemic, which could present serious animal welfare concerns
- Neighboring communities may be put at risk for pandemic influenza infection by proximity to sick pigs and/or infected swine workers;
- Demand for pork domestically may drop significantly as a result of public loss of confidence in its safety in the wake of a zoonotic swine influenza outbreak; and
- With 15% to as much as 25% of the current pork supply merchandised in export markets, the US swine industry risks huge financial losses should trading partners impose bans or additional restrictions³⁴³

US State	Case Count
Hawaii	1
Illinois	4
Indiana	138
Iowa	1
Maryland	12
Michigan	6
Minnesota	5
Ohio	107
Pennsylvania	11
Utah	1
West Virginia	3
Wisconsin	20

Table 6. Human infections with swine influenza virus, 2011-2012

Human outbreaks of SIV through 2012

The most significant outbreak of SIV in humans in the United States occurred between 2011 and 2012 and was caused by an A(H3N2)v virus. A total of 315 cases were reported with 16 hospitalizations and 1 death. A total of 13 states reported cases, with the majority split between Indiana and Ohio. All individuals reported direct or indirect contact with swine, primarily at agricultural fairs. The median case age was 7 years. This outbreak reinforced previous serologic study findings that children are less likely to have cross-reactive antibodies against a novel flu strain compared with adults. Evidence of limited person-to-person spread was documented. Rapid antigen point-of-care assays were unable to accurately detect these cases, reinforcing the need for confirmatory polymerase chain reaction testing, especially when influenza is suspected outside of typical seasonal prevalence periods.³⁰⁰

Before 2012, an average of 1 case of novel influenza A occurred every 1-2 years, primarily in those with direct or indirect contact with swine.⁶⁶ SIV poses no risk of infection when properly cooked swine meat is consumed by humans.⁶⁶

The [FluView](#) novel influenza dashboard only extends 10 years into the past. This CDC site contains detailed case reports of novel infections before 2013: [Reports of Human Infections with Variant Viruses](#).

[Human infections of SIV after 2012-2017 - U.S.](#)

The second largest human outbreak of novel influenza to date in the U.S. occurred in 2017 and was also attributed to an A(H3N2)v virus. Swine exposure at Maryland agricultural fairs resulted in 40 cases, 30 of which occurred in persons at increased risk for serious influenza complications. The majority of cases had direct contact with swine. An important finding from this outbreak was the need to extend mitigation measures and provide enhanced surveillance to all nearby agricultural fairs.³⁴⁶

[Human outbreaks of SIV- U.S. and international](#)

SIV infections in humans are tracked internationally by the WHO in the same way that AIV infections in humans are tracked: through [semimonthly human-animal interface reports](#). SIV infections in people, while sporadic and rarely involving person-to-person spread, occur more often than AIV infections in people and in a greater number of countries.^{12,347} Given the widespread distribution of swine facilities, predominance of the industry internationally, and the endemicity of influenza in swine, occasional transmission of an SIV to humans is not surprising. As evidenced by the 2009 A(H1N1)pdm09 pandemic, SIV has significant pandemic potential and must be monitored closely.

In 2021, 21 human cases (A(H1N1)v = 19, A(H3N2)v = 2) of SIV were reported in 9 countries (United States, Denmark, Canada, France, Taiwan, Austria, Australia, Germany, and China). A significant proportion of SIV human cases are identified in the United States, possibly because of the extensive surveillance, testing, and reporting, but also because of the extensive interaction between humans and swine, whether through production, farm exposure, agricultural fairs, etc.³²⁹ Four U.S. states reported cases in 2021-2022—Ohio, Iowa, Wisconsin, and North Carolina—all with robust swine industries.¹⁸⁶ As previously stated in the Human Surveillance and Epidemiology section, human SIV infections vary greatly by year. A(H3N2)v cases were more common in previous years, but A(H1N1)v cases are now more prominent in the United States and internationally (Figure 26).²

	season												
	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	Total
Influenza A H1N1v	0	2	2	0	3	1	0	1	1	0	3	0	18
Influenza A H1N2v	0	4	0	0	0	3	4	14	0	0	4	1	30
Influenza A H3N2v	7	315	20	3	3	19	51	2	0	1	2	1	434
Influenza A H7N2	0	0	0	0	0	0	1	0	0	0	0	0	1
Influenza A H1v	0	0	0	0	0	0	0	0	0	0	0	1	1
Influenza A H5	0	0	0	0	0	0	0	0	0	0	0	1	1
Total	7	321	22	3	6	23	66	17	1	1	14	4	465

Figure 26. Novel influenza A virus infections in humans in the U.S., CDC FluView 2022²

Resources for managing suspected and confirmed outbreaks of SIV

Responding to outbreaks of SIV where swine morbidity and mortality exceed that of endemic influenza activity requires the coordination of USDA APHIS Veterinary Services and state animal health officials. The following is a list of contacts for USDA and state health officials, testing guidelines and forms, testing algorithms, laboratory contacts, and notification plans for a novel influenza A virus laboratory finding.

- [Swine influenza–OIE–World Organisation for Animal Health](#)
- [VS District Offices Points of Contact](#) and the [State Animal Health Official Directory](#)
- [Testing Guidelines, Forms, Submission Instructions](#)
- [Influenza A in Swine Testing Algorithm Instructions](#)
- [Participating NAHLN labs](#)
- [Notification plan for novel influenza A virus in swine laboratory finding](#)
- [Guidance for State and Local Health Departments for the Investigation of Human Infections with Novel Influenza A Viruses at the Animal-Human Interface](#)

Transmission (including interspecies risk)

Zoonotic transmission of SIV from swine to humans is uncommon, though certain groups of people are more likely to acquire an SIV infection due to their regular exposure to swine. Transmission to agriculture workers or those with routine direct contact with pigs (e.g., owners raising animals for fairs) is well documented.^{139,339,342,348} SIV spreads easily from infected herds to uninfected herds, also by people and equipment shared between infected and uninfected herds, or the introduction of new stock to an infected herd.³⁴³

Swine populations are also susceptible to exposure-related transmission of AIV from wild birds, especially waterfowl such as ducks. Infected wild birds shed virus in feces and sometimes for extended periods. Fecal contamination in a watering pond or other water sources, whether used for swine consumption or cleaning, can result in an exposure. Multiple reassortant strains have resulted from swine exposure to AIV.^{28,343,349,350}

Conversely, SIV from swine can infect birds, as evidenced by serologic findings of cH1N1 in turkeys as well as isolation of cH1N1, A(H1N2), and A(H3N2).^{6,28,111,351,352}

Marketing and Production Systems

There is no formal internationally recognized production sector classification document for swine as there is for poultry, but 3 different production systems are widely recognized.¹⁰⁷ Large-scale confinement producers are equivalent to the sector 1 poultry classification. Commonly used biosecurity measures in the production cycle of these operations include disease reporting, laboratory testing, and movement control.²⁴ Large producers follow defined production steps starting with farrowing, nursing, growing, and finishing, with tight timelines for transport and slaughtering required to maintain profitability. This production approach leaves the system vulnerable to shocks and exportation bans resulting from disease outbreaks.²⁴

Smaller swine producers are like the poultry sector 4 classification. These producers are common in rural and semiurban areas in Asia, Central America, and Africa. Their animals are primarily raised for household consumption or sale in local markets, are not transported during growth cycles, feed by scavenging, and are integral to subsistence farmers.³³⁴ While biosecurity measures are challenging to implement in this classification of growers, they are less vulnerable to the impacts of outbreaks because most animals are not kept for income generation.³³⁴

Europe has a unique sector of niche growers using organic production and traditional breeds. This market has the same biosecurity vulnerability as large-scale producers.¹³⁸

International market chains involve the exchange of feed, vaccines, carcasses, and live animals; therefore, an outbreak in 1 country can impact several others economically. Even smaller production countries have complex contracts and production cycles involving multiple growers, processors, wholesalers, and sellers, and even live markets. These interrelationships are challenging to trace during disease outbreaks, and the impacts of the disease may be far-reaching.²⁴

Prevention and Control

The core tenants of influenza control among swine include (1) facility management, (2) herd health management and biosecurity measures, and (3) vaccination.³⁴³

Biosecurity practices

Facility management includes using environmental cleaning and disinfectants, especially between herds or before the addition of new stock, as well as introducing new stock after quarantine. Influenza is vulnerable to many commonly used disinfectants and is likely to survive outside of living cells for less than 2 weeks, with the exception of fresh water at appropriate temperatures.^{24,158} Temperature control is also important as the virus is more stable in colder temperatures. Herd management may

include avoiding the introduction of pigs carrying the virus for at least 3 months without quarantine.³⁴²

Vaccination

Vaccination programs for SIV are common practice to elicit immunity and reduce the risk of infection and illness among swine herds. According to the USDA APHIS 2010 National Surveillance Plan for Swine Influenza Virus in Pigs, vaccine manufacturers and producers are challenged by continued antigenic drift and shift ([see previous section](#)) in circulating SIV subtypes. The need for rapidly updated, effective vaccines becomes more critical as new trivalent reassortant viruses emerge and diverge. SIV vaccination does not confer complete protection as the composition of the 3 commercially available autogenous (custom) vaccines cross-react with less than half of known circulating viruses. However, SIV vaccines reduce viral shedding and lessen the severity of infection. The SIV vaccine is effective against A(H1N1) and A(H3N2) SIV strains, and maternal antibodies provide some passive immunity to piglets.^{342,343}

Equine Influenza Surveillance, Epidemiology, Prevention & Control

Surveillance

Equine influenza is an OIE-listed disease and is reportable to the organization. Influenza is highly contagious in horses and has caused substantial animal and, therefore, economic loss when detected. Equine influenza is primarily caused by A(H7N7) and A(H3N8) virus subtypes.³³⁸

Epidemiology

Equine influenza virus (EIV) is highly transmissible among Equidae including horses, donkeys, and mules. Outbreaks and individual cases are caused by 2 influenza virus subtypes—A(H7N7) and A(H3N8)—though A(H3N8) has been the only identified cause of infection in equid for more than 10 years.^{252,338} Similar to influenza illness in humans, horses can spread infection before displaying clinical signs of illness. The virus is spread on contaminated clothing and equipment and between horses. International movement of horses poses a risk for introduction into the country of entry; however, most countries have strict import standards including testing and quarantine on arrival.³³⁸

Equine influenza cases and outbreaks happen regularly throughout the world. The largest outbreak of the past 10 years occurred in Mongolia in 2011 in which more than 75,000 cases of A(H3N8) were reported.^{186,252} Mongolian free-range horse herds are affected by large-scale outbreaks approximately every 10 years, resulting in a significant negative economic impact.²⁵² South and Central America have experienced consistent outbreaks in the last 10 years (Table 6). Europe and Asia (except Mongolia) regularly report sporadic cases and small outbreaks (Table 6).

Table 6. Cases of equine influenza virus reported to the OIE 2010-2020, by region and country excluding the U.S. OIE WAHIS, 2022

Year (20XX)	10	11	12	13	14	15	16	17	18	19	20	Sum
Africa												
Mali										202		202
Niger												
Nigeria									93	2984		3077
Sudan										693		693
Americas												
Argentina			240						371			611
Brazil	3	62	1382	12	7							1466
Chile		2	220				11		1569			1802
Colombia									5025	37		5062
Ecuador									111			111
Asia												
China (People's Rep. of)								36	77			113
Cyprus	8											8
India												
Indonesia									37			37
Israel				3				77				80
Malaysia						4						4
Mongolia		75208			50							75258
Saudi Arabia										88		88
Turkey				10								10
Europe												
Croatia						11						11
Estonia											2	2
Finland			1									1
Hungary			1	2	11							14
Ireland												
Italy										20	1	21
Latvia										30		30
Russia			7								9	16
Serbia							1					1
Spain		1	3							29		33
Switzerland									3			3
United Kingdom	10											10
Total	21	75273	1854	27	68	15	12	150	7249	4083	12	88764

Vaccination

Equine influenza vaccination is common in many countries, but like the challenge with vaccinating avian and swine species, it is difficult to match strains in circulation. Vaccination does not always prevent infection, though it can reduce the duration and severity of illness. The OIE convenes an expert panel at least annually to review surveillance data and make recommendations for vaccine composition.³⁴⁰

Canine, Feline, and Other Animal Influenza Surveillance, Epidemiology, Prevention & Control

Surveillance and Epidemiology

Surveillance of influenza in felines and canines may be passively reported to the US Department of Agriculture Animal and Plant Health Inspection Service (APHIS) and may also be captured internationally by the World Organisation for Animal Health (OIE). Most outbreaks, which usually impact animal shelters and boarding facilities, are managed by local or state health officials. The first identification of canine influenza virus (CIV) in the United States occurred in 2004 among racing greyhounds.³⁵³ Since then sporadic outbreaks have occurred, most recently in 2017 and 2021 among shelter dogs and in boarding, grooming, and daycare facilities in LA County, California.^{279,280} CIV was considered enzootic in Colorado, New Jersey, New York, Florida, and Pennsylvania, but CIV A(H3N8) has not been detected for about 2 years, suggesting elimination.^{84,354} Occasional CIV studies are funded by USDA.³⁵⁵

Feline infection with influenza A viruses (IAV) occurs infrequently and is most often associated with shelter cats. The last outbreak in the United States occurred in 2016-2017, with an avian-origin influenza virus subtype A(H7N2), which also infected and caused mild illness in 2 humans who had direct contact with infected cats.²⁸⁷

Detection of influenza viruses in other animals is facilitated by research efforts, as was the case in the identification of IAV in bats in Central America, or the investigation of isolated deaths or aggregate illness or death in animals.²⁹¹⁻²⁹³ Examples of these animals include harbor seals, songbirds, parakeets, and pandas.^{22,175,356} Another recent interspecies transmission incident occurred in the United Kingdom when 5 swans died at a rehabilitation center followed by the deaths of a fox and seals, which were believed to have been infected with A(H5N8) by the swans.²⁰⁹

Investigation and Reporting

Unusual illness or outbreaks of illness should be assessed by a veterinarian and reported to state and local animal health authorities if influenza is suspected. As the animal counterpart to CDC, the USDA can determine the type and strain of animal influenza virus infection. There are currently no known influenza viruses with sustained transmission in cats. However, humans can transmit influenza to cats or dogs regularly. Local and state human health officials should be notified immediately of the suspected spread of zoonotic IAV to humans: [How NNDSS Conducts Case Surveillance](#).

Risk Assessment

CIV is not actively circulating in US canine populations. Humans can transmit influenza to both cats and dogs, but transmission of influenza from these animals to people is rare.

See the following section on the [Influenza Risk Assessment Tool](#) for more information on the evaluation of animal influenza viruses for potential pandemic risk.

Vaccination

Vaccines are approved for use in dogs, but not in cats, for A(H3N8) and A(H3N2) subtypes separately and in bivalent formulation. Vaccination can reduce the risk of infection, severe illness, and death among canines, but may not prevent infection.³⁵⁷

Future Considerations for Zoonotic Influenza

In the U.S. in 2022, widespread detection of avian influenza in wild, migratory birds led to the largest ongoing outbreak of avian influenza among domestic poultry again threatening the stability of the poultry industry. This pathogen may become entrenched in avian populations presenting a new challenge in surveillance, detection, and mitigation of influenza. At the time of this writing, the first human case of avian influenza was confirmed in the U.S. in Colorado in a person with known contact with infected birds. While not an immediate threat, the prevalence of avian influenza in the U.S. presents a new opportunity for reassortment of the influenza virus.

In the last 20 years, there have been 3 new animal-to-human coronaviruses, including SARS-CoV-1, Middle Eastern Respiratory Syndrome, and SARS-CoV-2; a 2009 A(H1N1) influenza pandemic; an epidemic of Ebola; outbreaks of Zika virus; we well as other infectious diseases.³⁵⁸⁻³⁶² These events are increasing in frequency, diversity of pathogen type, global distribution of vectors and hosts, and in new animal species.

If lessons are to be learned from the COVID-19 pandemic, the early detection of a new viral respiratory pathogen and subsequent mitigation efforts are critical to reducing the impact on human and animal populations. The dynamic nature of how influenza viruses move through populations of animals, whether seasonally or in their acquisition of new genes, places influenza near the top of known diseases continually posing a threat to human and animal health.³⁵⁹ A [One Health](#) approach, which relies on collaborative, multisectoral, and transdisciplinary engagement to address health threats at the interface of human, animal, and environmental health, is needed to respond to these zoonotic events. Strengthening the U.S. and international public health systems is necessary to ensure the health and safety of current and future humans and animals.

Public Health Resources

General Influenza

- [Pandemic Influenza \(Flu\)|CDC](#)
- [Influenza \(Flu\)|CDC](#)
- [Weekly US Influenza Surveillance Report](#)
- [Understanding Flu Viruses](#)
- [What's New on This Site](#)
- [Influenza in Animals|CDC](#)
- [What CDC Does About Novel Flu: Outbreak Investigations](#)
- [Nonpharmaceutical Interventions \(NPIs\)|CDC](#)

Swine Influenza

- [Information on Swine/Variant Influenza](#)
- [Variant Influenza Viruses in Humans](#)
- [Swine Influenza \(Influenza in Swine\)](#)

Animal Exhibitors and Event Organizers

- [Measures to Minimize Influenza Transmission at Swine Exhibitions, 2018–NASAHO and NASPHV](#)
- [Information for Fair Organizers and People Exhibiting Pigs](#)
- [Video Podcast: CDC Recommendations to Reduce the Risk of H3N2v Flu Virus Infection for Fairgoers and Swine Exhibitors](#)
- [Swine Health Information Center](#)
- [Pork Checkoff](#)

Key Facts for People Exhibiting at Fairs

- [Key Facts for People Exhibiting Pigs at Fairs](#)
- [What People Who Raise Pigs Need to Know](#)

Producers and Farmers

- [Centers for Disease Control and Prevention \(CDC\): Information for Pork Producers and People Who Work With or Raise Pigs](#)
- [Information on Swine/Variant Influenza](#)
- [The Junior Disease Detectives: Operation Outbreak Graphic Novel](#)
- [Flu Can Spread Between Pigs and People \(cdc.gov\)](#)
- [Influenza and Zoonoses Education Among Youth in Agriculture Program \(cdc.gov\)](#)
- [Influenza Vaccine Selection for Pigs](#)
- [Avian Influenza—Control and Prevention|Occupational Safety and Health Administration \(osha.gov\)](#)

Public Disease Prevention Resources

- [National Pork Board Factsheet: INFLUENZA: Pigs, People, and Public Health](#)
- [Compendium of Measures to Prevent Disease Associated With Animals in Public Settings](#)
- [Take Action to Prevent the Spread of Flu Between People and Pigs](#)

Veterinary Resources

- [American Association of Swine Veterinarians \(aasv.org\)](#)
- [Measures to Minimize Influenza Transmission at Swine Exhibitions 2018 \(nasphv.org\)](#)
- [Optimal Use of Vaccines for Control of Influenza A Virus \(iastate.edu\)](#)
- [SHIC-factsheet-influenza-cd-27Sept2021.pdf \(swinehealth.org\)](#)
- [A-review-of-optimal-use-of-diagnostics-and-vaccines-for-control-of-IAV-S-veterinarian-handout \(iastate.edu\)](#)

Avian Influenza

- [Information on Avian Influenza|Avian Influenza \(Flu\) \(cdc.gov\)](#)
- [Avian Influenza in Birds|Avian Influenza \(Flu\) \(cdc.gov\)](#)
- [Avian Influenza A Virus Infections in Humans|Avian Influenza \(Flu\) \(cdc.gov\)](#)

USDA APHIS

State veterinarians & producers

- [Avian Influenza Guidance Documents](#)
- [Defend the Flock Program](#)
- [Defend the Flock—#FlockDefender Youth Program](#)
- [NPIP Animal Health \(poultryimprovement.org\)](#)
- [HPAI in Poultry: What to Expect if You Suspect](#)
- [HPAI: A Guide to Help You Understand the Response Process](#)
- [The HPAI Indemnity and Compensation Process](#)
- [Detection and Quarantine](#)
- [Appraisal and Compensation](#)
- [Depopulation and Disposal](#)
- [Eliminating the HPAI Virus](#)
- [HPAI and Vaccine Use](#)
- [Border Protection and Trade](#)
- [Food Safety and Avian Influenza](#)
- [Protecting Birds From Avian Influenza](#)
- [Strategies for Controlling Avian Influenza in Birds and Mammals—The Threat of Pandemic Influenza—NCBI Bookshelf \(nih.gov\)](#)

State public health veterinarians

- [Information for People Exposed to Birds Infected With Avian Influenza Viruses of Public Health Concern](#)
- [Public Health Monitoring Plan for USDA APHIS Responders to Detections of Avian Influenza Virus in Poultry](#)

General

- [Find a state extension service](#)
- [Pandemic Influenza—Overview|Occupational Safety and Health Administration \(osha.gov\)](#)
- [Foreign Animal Diseases: “The Gray Book”](#)
- [World Organisation for Animal Health \(OIE\)](#)
- [National Assembly of State Animal Health Officials \(NASAHO\) \(nasda.org\)](#)
- [NASPHV Zoonotic Influenza](#)
- [Measures to Minimize Influenza Transmission at Swine Exhibitions, 2018—NASAHO and NASPHV](#)
- [Guidance for State and Local Health Departments for the Investigation of Human Infections With Novel Influenza A Viruses at the Animal-Human Interface](#)

Other Animals

Equine

- [Equine Disease Communication Center](#)
- Universal Equine Microchip Lookup: www.horselookup.org
- [Equine Health Resources \(2016 Equine Health Forum\)](#)
- [USDA APHIS|Equine Information](#)

Canine, Feline, and Bats

- [Key Facts About Canine Influenza \(Dog Flu\)|Seasonal Influenza \(Flu\)|CDC](#)
- [Influenza in Cats|Seasonal Influenza \(Flu\)|CDC](#)
- [Bat Influenza \(Flu\)|Seasonal Influenza \(Flu\)|CDC](#)

Appendix A: Avian LPAI and HPAI Cases and Outbreaks by World Region and Country, 2005-2021

Year	World Region	Subtype	Cases	New Outbreaks	
2005	Africa	A(H5N2)		2	
		Asia	–	32	
	Europe	A(H5)	400	0	
		A(H5N1)	571150	1208	
		A(H7N7)	20336	3	
		–	4	3	
2006	Africa	A(H5N1)	23234	117	
		–	4	1	
		A(H5N1)	112663	1179	
	Asia	A(H5N2)	16	76	
		–	55	5	
		A(H5)	148086	4	
A(H5N1)		1508132	653		
2007	Europe	A(H7N1)		1	
		Other	15486	53	
		–	987	10	
	Americas	A(H5N1)	1434627	723	
		A(H5N2)	0	1	
		A(H5N3)		2	
2008	Africa	–	2	2	
		A(H5N1)	29320	465	
		A(H5N1)		1	
	Americas	A(H5N2)	3	4	
		A(H7N3)	540	1	
		A(H7N9)		1	
	Asia	–	85355	695	
		A(H5N1)	554098	363	
		A(H7N8)	10	2	
		Other	8079	6	
		Europe	A(H5)	2691	2
			A(H5N1)	57391	379
A(H5N2)			4		
2009	Europe	A(H7N2)	23	2	
		A(H7N3)	31761	18	
		A(H7N3)	72757	124	
	Americas	A(H5N2)	24	35	
		A(H5N8)		1	
		A(H7N3)		1	
	Asia	–	124965	1583	
		A(H5N1)	622699	2056	
		A(H5N2)	5570	5	
		Other	70	19	
		Europe	–	1	1
			A(H5N1)	219	7
A(H5N2)	2		2		
A(H5N3)	551		31		
A(H7N1)	7		3		
A(H7N7)	15000		1		

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2009	Africa	A(H5N1)	75792	168		
		Americas	A(H5N2)	1973	29	
			A(H7N9)		2	
	Asia	–	19334513	1896		
			A(H5N1)	108665	1157	
			A(H7N6)	10	7	
	Europe		Other	32686	41	
			A(H5N1)	571	4	
			A(H5N1); A(H7N1_	46	3	
			A(H5N2)	25	1	
			A(H5N3)	558	10	
			A(H5N7);not typed	25	3	
			A(H7N1)	23	6	
			A(H7N1);not typed	24	14	
			A(H7N3)	4	2	
			A(H7N3);not typed	126	8	
			A(H7N7)	30454	2	
			A(H7N9)	679	1	
	2010	Africa	A(H5N1)	62861	458	
			Americas	A(H5N2)	312	68
Asia		–	56212980	2497		
			A(H5N1)	111797	116	
			A(H5N2)	3061	4	
			A(H7N2)	7	2	
			A(H7N6);other	2	2	
			A(H7N7)	965	14	
			A(H7N7);other	160	2	
			Other	1432	43	
		Europe		A(H5N1)	467	4
				A(H5N2)	10	3
			A(H5N3)	20	1	
			A(H7N1)		2	
			A(H7N3)	1355	4	
			A(H7N4)		1	
			A(H7N7)		0	
			Not typed	13	3	
2011		Africa	A(H5N1)	218797	317	
				A(H5N2)	12678	44
			A(H5N2); A(H7N1)	1028	0	
	Americas		A(H5N2)	260	14	
			A(H7N3)		1	
			A(H7N9)		1	
	Asia	–	25652432	1275		
			A(H5N1)	327730	382	
			A(H5N2)	220	2	
			A(H5N2); A(H7N3)	41	2	
			Not typed	351	26	
			Other	11033	25	
		Europe		A(H5)	445	4
			A(H5); A(H5N2); A(H7)	18	3	
			A(H5); A(H7)	20	4	
			A(H5N2)	717	0	
	A(H7)		125	12		

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		A(H7N1)	10	1
		A(H7N7)	4354	25
2012	Africa	–		6
		A(H5N1)	26525	12
		A(H5N2)	3297	6
		A(H5N2); A(H7N1)	3393	11
		A(H7N1)	231	6
	Americas	A(H5N2)	195187	19
		A(H7N3)	2867884	46
	Asia	–	30263080	1945
		A(H5N1)	291810	147
		A(H5N2)	8778	17
		Other	3106	25
	Europe	A(H5)	434	3
		A(H5); A(H5N2)	25	2
		A(H5; A(H5N2); A(H7N2)	9	1
		A(H5); A(H7)	14	2
		A(H5N2)	103351	13
		A(H7)	12	2
		A(H7N7)		1
	Oceania	A(H5N3)		1
		A(H7)	5000	1
2013	Africa	–	5250	2
		A(H5N1)	179304	90
		A(H5N2)		0
		A(H5N2); A(H7N1)		0
		A(H5N2); A(H7N1); A(H7N7)	6410	5
		A(H5N2); A(H7N7)	4219	5
		A(H7)	4	1
		A(H7N10)	64	3
		A(H7N7)	2	2
	Americas	A(H5N2)	18000	157
		A(H7N3)	695594	64
		A(H7N7)		1
	Asia	–	15851155	1567
		A(H5N1)	601455	763
		A(H5N2)	12021	5
		A(H5N2); A(H5N3)	80	3
		A(H7)	2	1
		A(H7N9)	93	25
		Other	4165	49
	Europe	A(H5)	4	1
		A(H5); A(H5N2)	4121	5
		A(H5); A(H5N3)	40	2
		A(H5N1)	122	6
		A(H5N1); A(H7N7)	410	0
		A(H5N2)	7	2
		A(H5N3)	65	3
		A(H7)	3	1
		A(H7); A(H7N7)	256851	6
		A(H7N1)	5261	3
		A(H7N7)	284	7
	Oceania	A(H5)	1	1

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		A(H7)		0
		A(H7N2)	18620	2
2014	Africa	A(H5)	3300	1
		A(H5N1)	36853	151
		A(H5N2)		0
		A(H5N2); A(H7N1)	2583	5
		A(H5N2); A(H7N1); A(H7N7)	1176	4
		A(H5N2); A(H7N7)	5028	5
		A(H7N1)		0
		A(H7N7)		0
	Americas	A(H5N2)	20666	13
		A(H5N2); A(H5N8)	37	3
		A(H5N8)	28	2
		A(H7N3)	15137	7
	Asia	–	468732	1242
		A(H5)	20	1
		A(H5N1)	410096	402
		A(H5N1); A(H5N2); A(H5N6)	7	5
		A(H5N1); A(H5N3); A(H5N6)	4	3
		A(H5N1); A(H5N6)	8	7
		A(H5N2)	41	6
		A(H5N2); A(H5N3)		0
		A(H5N2); A(H5N6)	8	5
		A(H5N2); A(H5N8)	2	2
		A(H5N6)	29020	19
		A(H5N8)	40152	477
		A(H7N9)	2728	62
	Europe	A(H5)	5	1
		A(H5N1)	488	4
		A(H5N2)	3	3
		A(H5N3)		0
		A(H5N8)	13605	14
		A(H7)	131	1
		A(H7N1)	33	2
	Oceania	A(H7N2)		0
2015	Africa	A(H5)	2720	2
		A(H5; A(H5N1)	6912	5
		A(H5N1)	684072	716
		A(H5N2)	9309	26
		A(H5N2); A(H7N3)	3804	4
	Americas	A(H5); A(H5N1); A(H5N2)		0
		A(H5); A(H5N1); A(H5N2); A(H5N8)	95	0
		A(H5); A(H5N2)		0
		A(H5N1); A(H5N2)		0
		A(H5N1); A(H5N2); A(H5N8)	95	2
		A(H5N2)	41552	291
		A(H5N2); A(H5N8)	19	13
		A(H5N8)	10	11
		A(H7N3)	3262	6
	Asia	–	522526	1264
		A(H5)	24182	9
		A(H5); A(H5N1)	1628	1
		A(H5N1)	2484430	188

		A(H5N1); A(H5N6)	450	1
		A(H5N2)	84556	63
		A(H5N2); A(H5N3); A(H5N8)	715510	332
		A(H5N2); A(H5N6)	1616	1
		A(H5N2); A(H5N8)	285230	107
		A(H5N3); A(H5N8)	28	2
		A(H5N6)	36189	31
		A(H5N8)	679	367
		A(H7N9)		0
	Europe	–	102	1
		A(H5N1)	126	13
		A(H5N1); A(H5N2)	948	11
		A(H5N1); A(H5N2); A(H5N9)	3931	17
		A(H5N2)	174	12
		A(H5N2); A(H5N3)	8730	6
		A(H5N2); A(H7N2)	5	2
		A(H5N3)		1
		A(H5N8)	1994	7
		A(H5N9)		1
		A(H7)	52	1
		A(H7N7)	36976	6
2016	Africa	A(H5N1)	487507	436
		A(H5N1); A(H5N8)	33	1
		A(H5N2)	170	4
		A(H5N2); A(H7N2)	5254	4
		A(H5N2); A(H7N3)	1326	3
		A(H5N8)	121	3
		A(H7N1)	1300	1
	Americas	–	2890	150
		A(H5N1)		1
		A(H5N2)	13	3
		A(H7N3)	80596	28
		A(H7N6)	5534	1
		A(H7N8)		9
	Asia	–	42787	743
		A(H5N1)	616710	233
		A(H5N2)	114	1
		A(H5N2); A(H5N8)	72645	28
		A(H5N3); A(H5N8)		0
		A(H5N6)	206871	462
		A(H5N8)	408041	70
		A(H7N9)	1	1
	Europe	–	29	10
		A(H5N1)	2488	8
		A(H5N1); A(H5N2); A(H5N9)		1
		H5N1); A(H5N3)	115	2
		A(H5N1); A(H5N3); A(H5N8)		4
		A(H5N1); A(H5N9)		11
		A(H5N2)	8141	11
		A(H5N3)	26	7
		A(H5N5)	1	1
		A(H5N5); A(H5N8)	7	3
		A(H5N8)	360445	741

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		A(H5N9)	430	4
		A(H7N7)	2883	4
		A(H7N9)		1
2017	Africa	–	8043	7
		A(H5)		0
		A(H5N1)	51753	106
		A(H5N1); A(H5N8)	8746	38
		A(H5N2)		0
		A(H5N2); A(H7N2)	79	2
		A(H5N8)	522955	120
		A(H7)	1	2
		Other	6931	25
	Americas	A(H5N2)	18649	172
		A(H7); A(H7N9)		1
		A(H7N3)	10	1
		A(H7N6)	108	2
		A(H7N9)		6
	Asia	–	16544	91
		A(H5N1)	72839	185
		A(H5N1); A(H5N6)	50	1
		A(H5N1); A(H5N8)	6712	5
		A(H5N1); A(H7N9)	35000	0
		A(H5N2)	3034	3
		A(H5N2); A(H5N6)	1380	10
		A(H5N2); A(H5N6); A(H5N8)	101295	76
		A(H5N2); A(H5N8)	77707	64
		A(H5N2); A(H7N3)	6045	2
		A(H5N6)	282462	120
		A(H5N6); A(H5N8)	2476	141
		A(H5N8)	167342	65
		A(H7N3)	3700	1
		A(H7N9)	172384	9
		Not typed	33	
	Europe	A(H5)	7213	1
		A(H5N1)	80	8
		A(H5N1); A(H5N2)		3
		A(H5N1); A(H5N3)		3
		A(H5N1); A(H5N8)	1008	28
		A(H5N1); A(H5N9)		1
		A(H5N2)	55132	11
		A(H5N2); A(H5N3)		5
		A(H5N3)	2	7
		A(H5N5)	65	4
		A(H5N5); A(H5N8)	2365	3
		A(H5N6)		1
		A(H5N6); A(H5N8)	200	2
		A(H5N8)	1610257	900
		A(H5N9)		0
		A(H7)		1
		A(H7N9)		0
2018	Africa	A(H5); A(H5N1)	30639	3
		A(H5N1)	8367	37
		A(H5N1); A(H5N8)	2113	3

		A(H5N2)		0
		A(H5N2); A(H7N2)		0
		A(H5N8)	4644	42
	Americas	A(H5N2)	2345	97
		A(H7N1)		2
		A(H7N3)	6181	12
	Asia	–	46994	41
		A(H5)	4471	3
		A(H5); A(H5N2)	51438	53
		A(H5); A(H5N2); A(H5N8)	10177	11
		A(H5N1)	91932	258
		A(H5N2)	14481	35
		A(H5N2); A(H5N6)		1
		A(H5N6)	57293	32
		A(H5N8)	754927	43
		A(H7N9)	17012	5
	Europe	A(H5)	5504	4
		A(H5N1)	1	1
		A(H5N1); A(H5N2); A(H5N5)		1
		A(H5N2)	416439	5
		A(H5N2); A(H5N3)		2
		A(H5N3)		18
		A(H5N6)	150	2
		A(H5N7)	10	1
		A(H5N8)	510069	108
		A(H7N7)		2
2019	Africa	–	3215	8
		A(H5N1)	22332	19
		A(H5N1); A(H5N8)	1010	4
		A(H5N2)	10	1
		A(H5N6)		0
		A(H5N8)	2305	41
		A(H7N2)	75	1
	Americas	A(H5)		0
		A(H5); A(H7N3)		1
		A(H5N2)	27652	113
		A(H5N9)		1
		A(H7N3)	19087	33
		A(H7N6)	95649	4
	Asia	–	82095	57
		A(H5)	2899	1
		A(H5); A(H5N2)	1222	2
		A(H5); A(H5N2); A(H5N5)	4913	6
		A(H5N1)	59400	277
		A(H5N2)	51337	88
		A(H5N2); A(H5N5)	4923	13
		A(H5N5)	1708	2
		A(H5N6)	12494	10
		A(H5N8)	94893	10
		A(H7N4)		0
		A(H7N7)		1
	Europe	A(H5)	11580	5
		A(H5N1)		2

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		A(H5N3)		1
		A(H5N8)	70693	7
		A(H7N3)	1354	1
		A(H7N7)		1
2020	Africa	A(H5N1)	70178	11
		A(H5N1); A(H5N8)	1726	
		A(H5N8)	8273	14
		A(H7)	172	12
		A(H7N8)	805	1
	Americas	A(H5)		
		A(H5N2)	616	17
		A(H7N3)	237	15
	Asia	A(H5)	69828	19
		A(H5N1)	22885	24
		A(H5N2)	39711	27
		A(H5N5)	53222	49
		A(H5N6)	47633	60
		A(H5N8)	380441	110
		Not typed	123595	14
	Europe	A(H5)	198254	38
		A(H5N1)	150	2
		A(H5N3)	4	1
		A(H5N5)	104	3
		A(H5N8)	925043	509
		A(H7N1)	14300	2
	Oceania	A(H5N2)		2
		A(H7N6)	2000	1
		A(H7N7)	255012	3
2021	Africa	A(H5N1)	1268	3
	Asia	A(H5N1)	995	4
		A(H5N6)	28281	35
		A(H5N8)	1147509	114
		Other	18218	26
	Europe	–	1241	7
		A(H5)	31	2
		A(H5N1)	7383	6
		A(H5N3)	12344	4
		A(H5N5)	84	3
		A(H5N8)	887498	377
		A(H7N7)	34	1
Grand Total			177,744,250	37,889

Appendix B. Contact List

CDC Influenza Division

The CDC Influenza Division has an emergency contact line staffed 24/7.

CDC INFO: [Contact CDC-INFO](#); 800-CDC-INFO (800-232-4636), TTY: 888-232-6348

CDC Influenza Division: 404-639-3747

National Veterinary Services Laboratories (US Department of Agriculture [USDA] Animal and Plant Health Inspection Service [APHIS] District Offices)

NVSL FADDL		NVSL AMES	
Main Office	(631) 323-3256	NVSL Director	(515) 337-7301
AFTER HOURS AND WEEKENDS		Diagnostic Virology	(515) 337-7551
Diagnostic Services Section Head	(631) 375-5314	Pathobiology	(515) 337-7526
Acting Diagnostic Services Section Head	(631) 405-0218	Diagnostic Bacteriology	(515) 337-7568
Courier	(631) 566-0073	AFTER HOURS AND WEEKENDS	
NPIC (M-F, 8:00 AM – 4:30 PM ET)		Nat'l Centers for Animal Health Dispatch	(515) 337-7200
Jon Zack	(240) 252-8074	APHIS VS DISTRICT OFFICES	
Julie Gauthier	(919) 219-8433	District One	(508) 363-2290
Barbara Porter-Spalding	(919) 637-4409	District Two	(352) 313-3060
Nathan Birnbaum	(240) 508-9888	District Three	(517) 337-4700
AFTER HOURS AND WEEKENDS		District Four	(512) 383-2400
NPIC/NVS 24/7 Emergency Answering Service	(800) 940-6524	District Five	(970) 494-7400
		District Six	(916) 854-3950

NASPHV State Public Health Veterinarians Contact List

[StatePublicHealthVeterinariansByState.pdf \(nasphv.org\)](#)

National Assembly of State Animal Health Officials

[National Assembly of State Animal Health Officials \(NASAHO\) \(nasda.org\)](#)

United States Animal Health Association (USAHA)

[State Animal Health Officials](#)

State Contact Representatives and Key Contacts (National Poultry Improvement Plan)

[OfficialStateAgencies.pdf \(poultryimprovement.org\)](#)

State 24 /7 after hours epi-on call contact numbers for all states

https://cdn.ymaws.com/www.cste.org/resource/resmgr/poc/epioncall_update1622.pdf

State epidemiologists

<https://www.cste.org/page/StateEpi>

US Agencies

[United States Agency for International Development \(USAID\)](#)

[United States Department of Agriculture \(USDA\)](#)

[Animal and Plant Health Inspection Service](#)

[Food Safety and Inspection Service](#)

[United States Department of the Interior](#)

[United States Geological Survey](#)

[National Wildlife Health Center](#)

[United States National Park Service](#)

[United States Fish and Wildlife Service](#)

[National Oceanic and Atmospheric Administration's Oceans and Human Health Initiative \(NOAA\)](#)

International

[Food Agriculture Organization of the United Nations \(FAO\)](#)

[World Health Organization \(WHO\)](#)

[World Organisation for Animal Health \(OIE\)](#)

Professional Organizations

[American Veterinary Medical Association \(AVMA\)](#)

[Association of American Veterinary Medical Colleges \(AAVMC\)](#)

[Pet Industry Joint Advisory Council \(PIJAC\)](#)

[National Association of State Public Health Veterinarians \(NASPHV\)](#)

[United States Animal Health Association \(USAHA\)](#)

[World Small Animal Veterinary Association \(WSAVA\)](#)

One Health Partners

CDC One Health website: <https://www.cdc.gov/onehealth/index.html>

USDA APHIS One Health

website: <https://www.aphis.usda.gov/aphis/ourfocus/onehealth>

[One Health Commission](#)

[One Health Initiative](#)

Appendix C. Influenza Viruses Evaluated Using IRAT Since 2010, CDC

Influenza Virus	Month and Year of Risk Assessment	Potential Emergence Estimate	Potential Impact Estimate	Risk Score Category
A(H5N6) clade 2.3.4.4b [A/Sichuan/06681/2021]	Oct.-2021	5.3	6.3	Moderate
A(H5N8) clade 2.3.4.4b [A/Astrakhan/3212/2020]	March-2021	4.6	5.2	Moderate
A(H1N1) [A/swine/Shandong/1207/2016]	July-2020	7.5	6.9	Moderate
A(H1N2) variant [A/California/62/2018]	July-2019	5.8	5.7	Moderate
A(H3N2) variant [A/Ohio/13/2017]	July-2019	6.6	5.8	Moderate
A(H9N2) Y280 lineage [A/Anhui-Lujiang/13/2018]	July-2019	6.2	5.9	Moderate
A(H7N9) [A/chicken/Tennessee/17-007431-3/2017]	Oct.-2017	3.1	3.5	Low
A(H7N9) [A/chicken/Tennessee/17-007147-2/2017]	Oct.-2017	2.8	3.5	Low
A(H7N8) [A/turkey/Indiana/1573-2/2016]	July-2017	3.4	3.9	Low
A(H7N9) [A/Hong Kong/125/2017]	May-2017	6.5	7.5	Moderate-high
A(H3N2) [A/canine/Illinois/12191/2015]	June-2016	3.7	3.7	Low
A(H5N6) [A/Yunnan/14564/2015] - like	April-2016	5	6.6	Moderate
A(H7N9) [A/Shanghai/02/2013]	April-2016	6.4	7.2	Moderate-high
A(H5N1) [A/American green-winged teal/Washington/1957050/2014]	March-2015	3.6	4.1	Low-moderate
A(H5N2) [A/Northern pintail/Washington/40964/2014]	March-2015	3.8	4.1	Low-moderate
A(H5N8) [A/gyrfalcon/Washington/41088/2014]	March-2015	4.2	4.6	Low-moderate
A(H9N2) G1 lineage [A/Bangladesh/0994/2011]	Feb.-2014	5.6	5.4	Moderate
A(H10N8) [A/Jiangxi-Donghu/346/2013]	Feb.-2014	4.3	6	Moderate
A(H3N2) variant [A/Indiana/08/2011]	Dec.-2012	6	4.5	Moderate
A(H7N7) [A/Netherlands/219/2003]	June-2012	4.6	5.8	Moderate
A(H1N1) [A/duck/New York/1996]	Nov.-2011	2.3	2.4	Low
A(H5N1) Clade 1 [A/Vietnam/1203/2004]	Nov.-2011	5.2	6.6	Moderate

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