ZOONOTIC INFLUENZA

Detection, Response, Prevention and Control Reference Guide

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CSTE
COUNCIL OF STATE AND TERRITORIAL EPIDEMIOLOGIST

Contents

Contributors

The first version of 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. The report content was prepared by Dr. Meghan Schaeffer. The project's primary sponsors were Dr. James Kile with the CDC Influenza Division and Ashley Vineyard of CSTE. The CSTE Zoonotic Influenza Workgroup provided regular feedback in workgroup meetings and general project support. Other subject matter experts from the National Association of State Animal Health Officials (NASAHO) contributed as needed.

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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; the guide 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.

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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 preparing and responding to emerging situations involving animal and zoonotic influenza viruses. The content was obtained through an extensive review of textbooks, journal articles, and web sources 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 online resources are provided. All citations are hyperlinked to their positions in the bibliography (ctrl+click or comm + click).

Table 1 Acronyms List

AIV	Avian Influenza Virus
CDC	Centers for Disease Control and Prevention
CIV	Canine Influenza Virus
CMS	Centers for Medicare and Medicaid Services
CSTE	Council of State and Territorial Epidemiologists
EIV	Equine Influenza Virus
FAO	Food and Agriculture Organization of the United Nations
Gs/GD	A/goose/Guangdong
HA	Hemagglutinin
HPAI	Highly pathogenic avian influenza
IAV	Influenza A Virus
IBV	Influenza B Virus
ICV	Influenza C Virus
IDV	Influenza D Virus

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Table 1 Acronyms List *(continued from previous page)*

IHR	International Health Regulations
ILI	Influenza-like illness
IRAT	Influenza Risk Assessment Tool
LPAI	Low pathogenic avian influenza
M1	Matrix protein
M2	Matrix ion channel
NA	Neuraminidase
NCHS	National Center for Health Statistics
NP	Nucleoprotein
NPIP	National Poultry Improvement Plan
NREVSS	National Respiratory and Enteric Virus Surveillance System
NS1	Nonstructural protein
NS2	Nonstructural protein 2
PA	Polymerase acidic (PA) subunits
PB1-F2	Accessory protein
pdm	pandemic (strain)
RSV	Respiratory syncytial virus
SAHO	State Animal Health Officials
SIV	Swine Influenza Virus
USDA	U.S. Department of Agriculture
USDA APHIS	U.S. Department of Agriculture, Animal and Plant Health Inspection Service
USGS	U.S. Geologic Survey
WHO	World Health Organization
WHO GISRS	WHO Global Influenza Surveillance and Response System
WOAH	World Organisation for Animal Health
WOAH-WAHIS	World Organisation for Animal Health – World Animal Health Information System

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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.[10,11] Influenza A viruses (IAVs) are significant pathogens of humans and animals. All influenza A and B viruses contain 8 genomic segments coding for 11 proteins, including the following[10]:

- 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 the A and B strains.[7,12-14] Influenza viruses have single-stranded ribonucleic acid (RNA) negative-sense genomes.[14,15]

Influenza A Viruses

Influenza A viruses (IAVs) are known to widely circulate in humans, wild birds, domestic birds, swine, equids, canines, and bats, with the potential to cause seasonal and sporadic epidemics in humans and swine.[16-26] Infections have increasingly occurred in marine animals, ostriches, pandas, and other animals, especially with the recent avian influenza A(H5N1) clade 2.3.4.4b global outbreak. IAVs are differentiated into subtypes based on their surface proteins.[16,17,24,25] Within the genera of IAVs, subtypes for HA and NA extend to 18 subtypes for HA and 11 for NA.[10] 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 additional host cells.[10,11,27,28]

More than 130 IAV subtypes have been identified in nature, with most found in avian species.[7] With the exception of H17, H18, N10, and N11, all probable combinations have been found in birds. Almost all IAV subtypes were originally isolated from avian hosts, with the exception of the 2 known bat IAVs (Figure 1).[7,11]

Wild aquatic birds are the natural reservoirs of IAVs. While IAVs have been isolated from more than 100 species of birds, ducks and mallards are the most common sources, followed by gulls and shorebirds.[29] 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.[15] 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.[30]

Human IAVs have only acquired new genetic segments from avian or other sources during the 4 major pandemic events in the last 100 years.[31] Outside 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 when a novel infection with IAV appears in swine.[32]

Influenza A is also endemic in swine populations. Influenza was first detected in swine in 1930

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Figure 1 Reports of influenza A virus hemagglutinin (HA) and neuraminidase (NA) subtypes by species, Source: Mostafa, et al., 2018.[7] Current data on subtypes in species are located at Influenza A Subtypes and the Species Affected | Seasonal Influenza (Flu) | CDC and WAHIS (woah.org)

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

following the 1918 pandemic, and it was confirmed as A(H1N1).[33] Swine have been the source of sporadic human infections with swine influenza viruses but were not considered a pandemic threat until an outbreak occurred among military recruits at Fort Dix (New Jersey) in 1976.[34] 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.[35-37]

Influenza B Viruses

Influenza B viruses (IBVs) are isolated almost exclusively from humans. Infection has also been detected in seals, which may serve as a reservoir.[25,38] Like influenza A, IBVs have 8 discrete gene segments, each coding for at least 1 protein.[7]

IBVs are defined by lineage, not by 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.[11] The HA gene of an IBV evolves at a much slower rate compared to the HA genes of an 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; it could be that the 2019 SARS-CoV-2 pandemic is pushing the virus to extinction, given that the B/Yamagata lineage has been detected only minimally since April 2019.[11,33,39]

Influenza C Viruses

Influenza C viruses cause cold-like symptoms in humans and occasionally, lower respiratory infections in children younger than 2 years of age. ICV infections cause mild illness in humans and are not known to cause epidemics.[11] Like influenza B, influenza C is found primarily in humans, though it can also be found in dogs, cattle, and swine.[34,38,40,41] Serologic studies show evidence of prior infection in up to 90% of children 7 to 10 years of age, suggesting widespread exposure to ICV in human populations.[42]

Influenza C viruses have only 7 gene segments and a single surface glycoprotein, hemagglutinin-esterase-fusion (HEF), which combines the functions of HA and NA.[10]

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Influenza D Viruses

Influenza D viruses (IDVs) affect cattle, other ruminants, and swine.[11,43-46] Discovered in 2011 in swine in Oklahoma, IDVs have subsequently been detected in multiple animal species.[34] Bovids are considered the major reservoir for IDVs, which may play a role in bovine respiratory disease. Seroprevalence surveys show up to 77% positivity, with the highest rates occurring in the upper Midwest and Mountain West.[43,47] IDVs are not known to infect or cause disease in people; however, the zoonotic potential of influenza D is controversial as cattle workers havedemonstrated serologic evidence of IDV infection.[11,43-46]

Like influenza C, IDVs have the HEF protein, which is functionally equivalent to the HA and NA glycoproteins. There are 2 lineages of influenza D: D/OK (location of initial identification) and D/Japan.[43]

Influenza A Naming Conventions

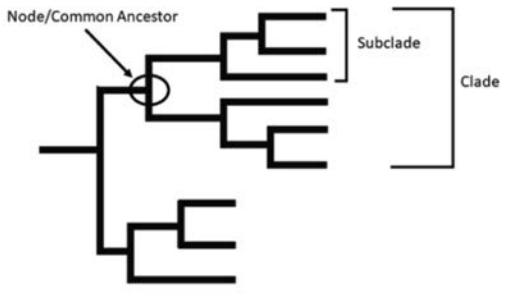
For more than 40 years, influenza virus naming conventions have followed an internationally accepted standard.[4,48] Each IAV name contains the antigenic type (A), the host species of origin (e.g., swine or equine) if the original host is nonhuman, geographical origin (e.g., California or Tokyo), strain number (not related to the HA or NA subtype), and year of collection.[11,48,49] 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 pandemic virus was named A(H1N1)pdm09.[49] 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).[11]

Genetic Sequencing of Influenza Viruses

Genetic sequencing, the process of determining the order of nucleotides (i.e., A, C, G, and U) in influenza viral RNA, is performed on approximately 7,000 specimens per year by CDC and National Influenza Reference Centers.[4,50] The comparison of viral sequences helps reveal changes to genes that code for the amino acids that make up viral proteins. Some genetic changes can result in structural modification of a protein, which may affect a virus's transmissibility, pathogenicity, and ability to "evade human immunity, spread between people, and susceptibility to antiviral drugs."[51] Genetic characterization is the process of comparing genetic sequences and assessing how closely viruses are related to one another, how they are evolving, viral properties associated with a particular genetic change (such as susceptibility to vaccination or treatment), and a virus's ability to infect species, including humans.[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 are 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 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. Clades and subclades are used to help flu experts track and monitor which viruses from different clades are in circulation. This approach to such a detailed characterization of influenza types is in response to the extensive genetic evolution and reassortant ability of IAV.[4,52]

Figure 2 Phylogenetic tree example. Source: CDC, Types of Influenza Viruses, 2021.[4]



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Clades and subclades are genetically different but may not be antigenically different. Antigens are molecules on the surface of viruses that can trigger a response by the immune system. Two flu viruses that are antigenically different may illicit different immune responses; and sometimes, one virus may illicit an immune response whereas another may not, even though both viruses are flu viruses. Therefore, an examination of which genes are different between clades or subclades is important in determining whether a virus causing infection in one clade will provide any immunologic protection against another virus from a different subclade.[4]

Additional information on genetic sequencing may be found online at 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).[7,11] The culprit in making replication errors is polymerase or the proofreading function in viral RNA replication.[52,53] 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.[54]

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. This results in the replicated genome varying from the "parent" genetic material being copied.[52,53] 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 that are fitter than the last, changes that arise through antigenic drift do not typically result in significant changes to the functionality of the virus.[52,53]

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 by considerable genetic reassortment.[10] With interspecies transfer, a virus develops or can adapt or acquire a receptor affinity that enables it to more easily infect a new species. Reassortment typically results from the 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.[53] Even with extensive study of animal reservoirs, it is extremely difficult to predetermine the antigenicity and virulence of a reassorted virus.

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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.[51,55] 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.[56,57] On average 8% of the US population (range 3%–11%) experiences influenza illness every year.[58] Influenza A and B strains circulate seasonally, with the A strain typically causing more severe illness. In temperate countries, the virus circulates during winter months, while in tropical and subtropical countries, year-round infections are present, 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.[52,59]

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 symptoms of fatigue and weakness may last for longer.[53,60] 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.[60]

Symptom onset typically occurs approximately 2 days following exposure, with the incubation period ranging from 1 to 4 days. An infected person may be contagious as early as 1 day before symptoms appear through 5 to 7 days after illness onset (i.e., infectious period), but are generally most contagious 3 to 4 days after the onset of symptoms. Immunocompromised, older (over 65 years of age), and younger (less than five years of age) people may be contagious for longer than 5 to 7 days.[58]

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.[61,62]

Prevention and Treatment

Vaccination is the most effective way to prevent influenza. Vaccination reduces the incidence of infection and, when it does occur, can result in milder influenza illness, shorter duration of illness, and a reduced risk of hospitalization and death. As of 2023, 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).[60,63,64] Everyone 6 months and older is advised to get an annual flu vaccine, preferably by the end of October.[60,63]

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.[65] 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.

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Dominant Influenza Subtypes in Humans

Human immunogenicity to seasonal influenza over the past 100 years has generally involved the hemagglutinin (HA) subtypes H1, H2, and H3.[66] 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.[67,68]

Humans are immunologically naïve to the A(H5), A(H7), and A(H9) subtypes, which is why these avian influenza virus subtypes are of significant concern. If any of these strains acquired the ability to spread easily from person to person, a global pandemic could ensue.[69]

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."[70] 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 an outbreak, which is an epidemic in a relatively limited geographic area.[71]

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.[72] Virus identification was available after 1932, and it was after this time that patterns in how pandemics affected seasonal influenza were established.[72] Each major pandemic and 1 epidemic changed the influenza strains that circulated, a pattern that continues today.[72-76]

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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.[77-79]

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.[76,80] 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.[72,81] 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.[78]

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.[54,78,82] 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.[73] 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.[72] This virus continued to circulate for 10 years after the pandemic, producing one major epidemic before the next pandemic in 1968.[72] With the arrival of the A(H2N2) strain, A(H1N1) disappeared from human infections until 1977.[83]

1968—H3N2 (Hong Kong Flu)

H3N2 arose from the genetic reassortment of low pathogenic 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.[74,78] 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 deaths.[72,74] This is 1 of the 2 human seasonal IAVs still in circulation today.

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

A novel A(H1N1) virus was detected in 230 military recruits at Fort Dix, New Jersey, and caused 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.[84] 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.[83,85]

1977 – H1N1 (Russian Flu) – Notable Epidemic

Russian flu, a reemergent A(H1N1) strain, caused severe human infections in persons younger than 26 years, resulting in a 50% fatality rate among children.[26,86,87] Case rates were estimated at fewer than 5 per 100,000, which was far less than any preceding pandemic or interpandemic event.[88] In 1977, individuals younger than 26 years had not been exposed to an A(H1N1) strain, as its last wide circulation occurred before 1957.[88] 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.[78,79] The strain is believed to have leaked from a laboratory.[30,89,90] 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.[91]

2009 – H1N1

In April of 2009, 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.[37,83,88] The first 2 patients were children who resided in California. Both displayed symptomatic illnesses, which were identified when their influenza viruses could not be subtyped and were sent to CDC for further testing. CDC identified both specimens as A(H1N1) swine-origin, but the cases had no epidemiologic links to each other. Additional cases were rapidly confirmed in the United States, Mexico, and Canada. More than 60% of the early case-patients were of school age; 16% of cases were from school-based outbreaks. Of patients with epidemiologic data, 18% had recently traveled to Mexico.[88,92,93]

The United States experienced an estimated 60.8 million cases, ~300,000 hospitalizations, and 12,500 deaths. CDC estimated between 151,700–575,400 people died globally. A(H1N1) pdm09 affected a much younger cohort of people compared to seasonal flu. Globally, over 80% of deaths in the first year of the pandemic were identified in people younger than 65 years of age; however, fatality rates for this pandemic were significantly lower than those in previous pandemics.[94] A(H1N1)pdm09 continues to circulate as a seasonal influenza strain, as is the typical pattern of pandemic flu viruses.[75]

After several years of sampling, retrospective swine sample review, and genetic sequencing, researchers established that the pandemic likely evolved from central Mexico. Initially, Mexico seemed an unlikely site of origin, as no related swine viruses had been detected in Mexico or in the Americas prior to the pandemic. Swine virus sampling post-pandemic revealed extensive diversity in circulating strains, which included segments from Eurasia not previously found in the Americas. These new sequences contained key genetic components of the A(H1N1)pdm09 virus suggesting the virus had been circulating in pigs for more than a decade. Additional studies found that global trade routes of live swine supported movement of the virus from Eurasia and the United States to Mexico.[95]

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 3).[8,96]

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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 definitions provided in Table 1. In reports published by CDC, "novel" influenza A infections include those with swine and avian origins; until recently only swine-to-human transmissions were reported in the United States.[14] 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 the literature frequently refers to swine-to-human transmission.

The term "novel" is widely applied to events of human infections with animal influenza viruses.[87] To differentiate human infections with swine influenza virus from animal infections with swine influenza virus, the term "variant" is sometimes used, and a letter "v" for variant is added to the SIV subtype name (e.g., A(H1N1)v).[68,97] Known variant strains in the United States resulting in human infection include A(H1N1)v, A(H3N2)v, and A(H1N2)v.[69,98]

According to 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.[14]

Novel IAV detections in humans are of particular interest as they have significant potential to spread from person to person. The impact of these viruses depends on their species subtype. AIV human infections range from asymptomatic to severe, whereas SIV infections are typically asymptomatic or mild.[87] Incidents 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) the increasing distribution of highly pathogenic avian influenza (HPAI) viruses in birds.[8] Low pathogenic avian influenza (LPAI) A(H9N2)

Figure 3 Zoonotic influenza A virus (IAV) infections in humans. Source: Widdowson, et al., 2017.[8]

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.

[a]Includes Taiwan and Hong Kong SAR.

[b]Imported case(s).

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viruses are endemic in domestic poultry, primarily throughout Asia, the Middle East, and Africa.[26] They frequently co-circulate with A(H5) and A(H7) viruses and, since 2015, have caused an increasing number of human infections. 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.[99] A(H5) avian infection in humans can range from asymptomatic to severe, and while the frequency of human infections of A(H5) has slowed globally in recent years, more regions and countries are reporting human cases than ever before. In the United States, 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.[100]

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.[101] 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.[101] In addition, the World Organisation for Animal Health (WOAH) strives to outline standards for animal health management, quarantine, disease prevention, surveillance, and vaccine recommendations.[102] CDC One Health is the head of the WOAH 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.[103,104]

The effectiveness of animal and human surveillance systems depends on their ability to detect and respond to incidents as close as possible to the origin and onset of each event.[105] Interspecies transmissions of highly pathogenic or reassorted avian or swine influenza viruses have resulted in enormous mass culling of animals, damaging economies and individual livelihoods, as well as jeopardizing human health, whether in isolated cases or on a larger scale, as happened with the 2009 A(H1N1) pandemic.[105-108] 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 provided in a later section of this reference guide: Surveillance, Epidemiology, and Prevention and Control of Influenza.

Surveillance data summaries of novel IAVs in the United States are published on the CDC website: 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, even death. Most instances of zoonotic human infection with AIVs have resulted from direct or proximal contact with infected poultry. Subtypes of AIV known to infect humans include H3, H5, H6, H7, H9, and H10.[68]

Swine Influenza Viruses of Concern

Most human infections with swine influenza virus (SIV) are mild, with much less severe illness and fewer mortalities than infection with AIV.[67] The occurrence of a SIV infection in a human may be an isolated event; it does not typically involve a new or variant virus. Classifications of zoonotic human infections with 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). The term novel is widely applied to events of human infections with animal influenza viruses.[87] To differentiate human infections with swine influenza virus from animal infections with swine influenza virus, the term variant is sometimes used. Known variant strains in the United States resulting in human infection include A(H1N1)v, A(H3N2)v, and A(H1N2)v.

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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.[109]

> *According to CDC,[109]*
> *"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:[109]

*The **"Properties of the Virus"** category contains four of the 10 risk elements, including:*

1. ***Genomic analysis** is a measure of the extent of genetic diversity or presence of known molecular signatures important for human infections and disease.*
2. ***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.*
3. ***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.*
4. ***Antiviral treatment options** refers to the predicted effectiveness of influenza antiviral medications, such as oseltamivir, zanamivir, baloxavir, and M2 blockers.*

*The **"Attributes of the Population"** category contains three of the 10 risk elements, including:*

5. ***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.*
6. ***Disease severity and pathogenesis** measures the severity of illness caused by a particular influenza virus in people and/or animals.*
7. ***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.*

*The **"Ecology and Epidemiology"** category contains the final risk elements, including:*

8. ***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.*
9. ***Infections in animals** refers 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?*
10. ***Human infections** refers 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?*

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Viruses evaluated using the IRAT are listed on the CDC website[110]: Summary of Influenza Risk Assessment Tool (IRAT) Results. Extensive risk summaries are also included on the CDC site.

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 internationally[111]. For more information on how CDC supports international surveillance efforts, visit this site: Influenza Division International Program (cdc.gov).

For details on international tracking, reporting, and risk evaluation of influenza by WHO, see the International Surveillance of Human (Seasonal) Influenza section of this document.

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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.[21] The earliest isolation of an avian influenza virus occurred in 1961 in a tern in South Africa, followed by serologic evidence of infection in 1967.[53,112] Avian influenza viruses (AIVs) have played significant roles as the origin viruses for the 1918, 1957, and 1968 pandemics.[53]

Migratory waterfowl, particularly Anseriformes (ducks, mallards, or geese) and Charadriiformes (gulls and shorebirds), serve as reservoirs for IAVs and rarely experience symptomatic infection.[113] Influenza viruses are most often spread between wild and domestic birds via the fecal-oral route. 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 interspecies transmission. In these markets, numerous bird types and mammals—from diverse backgrounds—capable of being infected with and spreading influenza viruses are brought together and housed with one another prior to sale.[114]

The majority of influenza A subtypes can replicate in domestic ducks, especially low pathogenic avian influenza (LPAI) viruses, with inapparent infection, similar to their wild duck counterparts. Domestic poultry and game birds (e.g., quail, chicken, and turkeys) play an interesting role in influenza transmission. In addition to being infected and developing the disease, they can serve as intermediary processing hosts or "mixing vessels," because they possess both human- and avian-type receptors, α2,6 and α2,3, which are responsible for viral attachment and entry into host cells.[115] This ability differs by bird species. (The same mixing vessel capability is present in swine.[116]) Turkeys are highly susceptible to influenza virus infection, as they support the replication of most avian and mammalian influenza viruses.[115,117,118] Chickens and other domestic poultry are also highly vulnerable to influenza virus infection and have perpetuated H3, H5, H7, and especially H9 subtypes.[99,119-121]

Of greatest potential threats to human health are the A(H5) and A(H7) subtypes. While low pathogenic A(H5) and A(H7) subtypes 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.[26,121] From 2003–2022, A(H5N1) highly pathogenic avian influenza (HPAI) viruses caused 868 human infections, of which 457 were fatal.[122] 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.[108,123] 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.[124,125]

For more information on the role of IAV in avian species, see Influenza in Avian Species.

Avian Subspecies Differentiation

Wild Waterfowl

The main species of wild waterfowl serving as reservoirs for IAVs are Anseriformes (e.g., ducks, geese, and swans) and Charadriiformes (e.g., gulls, terns, and shorebirds).[26,126] Infection in these species occurs in the intestinal tract, with an exceptionally large concentration of virus excreted in the birds' feces. However, the development of disease and symptoms occurs in the respiratory tract.[26,30,52]

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Other Wild Avian Species

Primary species studied with regard to influenza include quail and wild turkeys[26,115,116] Strains detected include A(H7) and A(H9) viruses.[116,127,128]

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.

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 AIVs 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 4). Most migratory bird species use a single flyway to migrate during spring and fall, though some species cross multiple flyways.[1] Detections of American lineage A(H7) AIV have occurred in summer, fall, and winter, usually peaking in early winter.[129] Eurasian lineage A(H5) AIVs were first introduced to North America, resulting in a large HPAI outbreak from birds that had migrated from Asia to North America in 2014.[130]

Widely recognized international flyways include the Pacific Americas, Atlantic, East Atlantic, Black Sea/ Mediterranean, East Africa and West Asia, Central Asian, East Asian-Australian, and West Pacific (also referred to as the Pacific or Alaska flyway) (Figure 5).[131-133] These flyways span the length of the world from north to south and across numerous continental latitudes.

The 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) AIVs have been detected in wild birds in the Atlantic and Mississippi flyways.[87]

Frequent recurrence of HPAI in wild and domestic birds in Europe since 2006 resulted in increased

Figure 4 North American waterfowl migratory flyways. Source: USDA APHIS, 2017.[1]

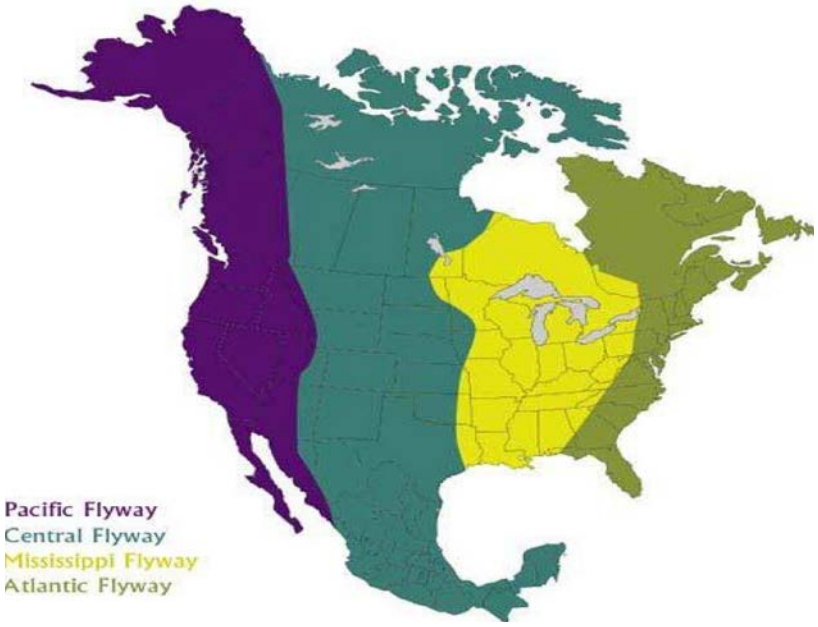

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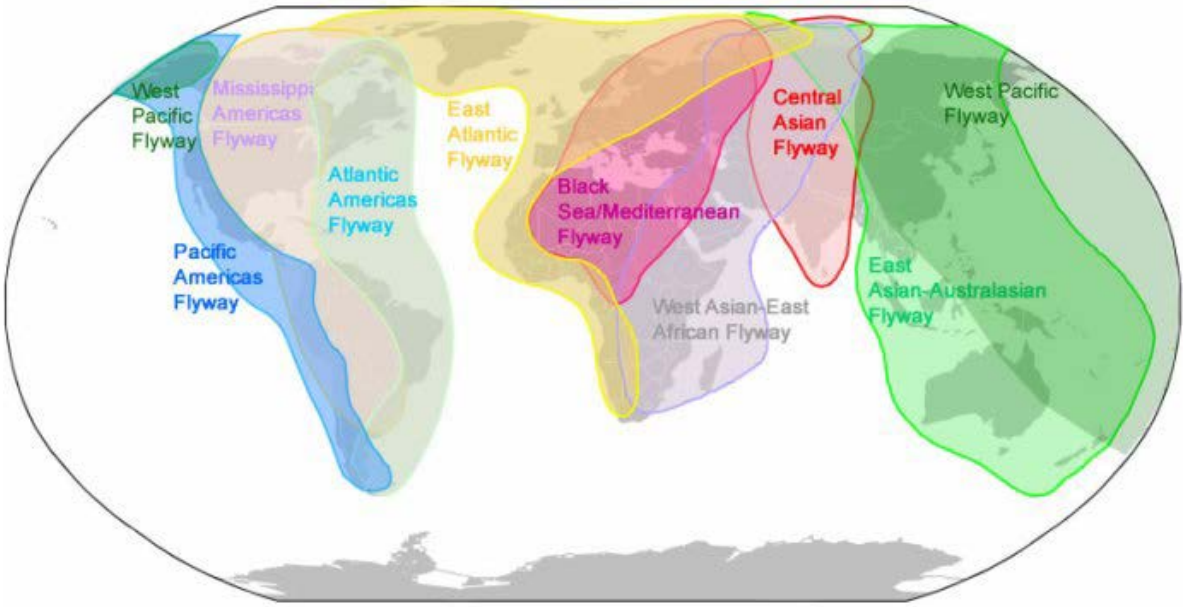
Figure 5 International bird migration flyways. Source: Migratory Birds Without Boundaries, 2022.[133]



coordination of surveillance in the North Atlantic.[15] Other significant factors contributing to the need for heightened surveillance in this region were raised by the U.S. Geological Survey (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[15]

Highly Pathogenic and Low Pathogenic Avian Influenza

Avian influenza viruses (AIVs) 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 pathogenic is related to the virus's ability to cause illness and death in domestic poultry and to produce genetic variation; it does not refer to the severity of illness in humans. Both HPAI and LPAI viruses have caused serious illnesses in humans.[13]

Wild waterfowl are known to be the reservoir for all AIVs; HPAI is thought to evolve in domestic poultry after transmission of LPAI from wild birds to poultry.[16,26,134] After domestic birds have been infected, a change in the hemagglutinin (HA) gene can occur, allowing the virus to mature in the respiratory tract and cause systemic infection.[26,54,135] The virus can also infect the gastrointestinal tract of birds, with minimal issues.[87] Once developed in poultry, HPAI can be transmitted back to wild birds. At present, HPAI is limited to the A(H5) and A(H7) subtypes.[26,53]

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The definition of infection with avian influenza according to WOAH, 2016 is the following[135]:

> *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 WOAH 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.[87]

HPAI H5N1 was first identified in 1996 in wild birds in China.[26,136] The first case of human infection was detected in 1997 in Hong Kong.[99] The impact of vaccination, strain evolution, and poultry immunologic adaptation from exposure has reduced poultry morbidity and mortality in recent years. Symptomatic outbreaks of HPAI happen among wild bird reservoirs, and infection in wild birds has increased in recent years.[14,137] Direct contact appears to be the most efficient method of transmission among infected poultry, though transmission most often occurs via fecal contamination of water, which is then ingested by uninfected animals; airborne transmission occurs less commonly.[120,138]

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.[11,16] There are additional supporting lineages named for viruses found in Australia and South America.[139,140]

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.[26,141] The most severe wave occurred in 2016–2017 with 759 human cases.[142-144] Limited, un-sustained person-to-person transmission was reported.[69]

In 2016, A(H7N9) avian viruses developed highly pathogenic capabilities. A total of 32 human infections were detected with the HPAI virus, later sequenced in poultry, which was the likely source of human infection.[145,146] A large-scale poultry vaccination program was implemented in China in September 2017 to protect against the A(H5) and A(H7) lineages, after which only 3 human cases of A(H7N9) were reported.[69,147]

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Evolution of Avian Influenza A(H5) HPAI Viruses

At the end of the 19th century and the 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. When they did occur, outbreaks of influenza were more commonly identified in turkeys, since turkeys were often raised in fewer enclosures and were allowed more open range than chickens. Turkey management practices changed because of the threat of avian influenza which resulted in the now-widespread use of enclosures, thereby reducing the number of outbreaks in turkeys.[148] Genetic characterization or subtyping was not widely available on samples from wild or domestic bird outbreaks before 1990.

Emergence of Highly Pathogenic Avian Influenza in Asia

In 1996, a unique lineage of A(H5N1) was detected in domestic geese in China.[26,136,149] 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.[99,150] In the years after its discovery, HPAI continued to cause outbreaks in domestic poultry, resulting in almost 100% morbidity and a high rate of mortality despite massive, multiyear efforts to contain the virus. For the first 7 years after 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 6).[151]

In 2005, an outbreak of Gs/GD A(H5N1) resulted in the deaths of more than 6,000 wild aquatic birds.[152] That same year, the virus was detected in wild birds in Europe.[26] Between 2006 and 2009, the Gs/Gd lineage A(H5N1) was detected in both domestic and wild birds in an additional 38 countries, with different clades developing in various countries (Figure 5).[87,153]

Sporadic outbreaks of Eurasian and Asian lineage A(H5) viruses among wild and domestic birds continued in Asia and Europe between 2010–2013.[154-156] In 2010, a genetically distinct clade 2.3.4.4 Gs/GD A(H5N1) lineage HPAI virus emerged, resulting in an increased occurrence of HPAI in wild birds (Figure 7).[157] The clade 2.3.4.4 virus became better adapted to waterfowl and was then able to cause asymptomatic infections in wild birds.[158]

Figure 6 Timeline of magnitude and occurrence of highly pathogenic avian influenza (HPAI). Source: Ramey et al., 2022.[137]

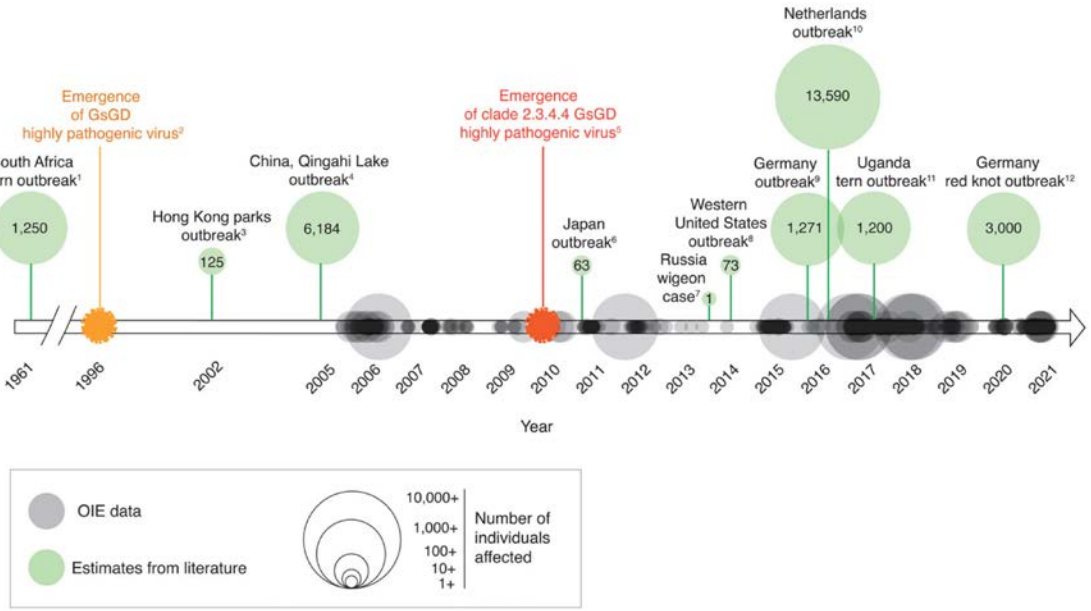

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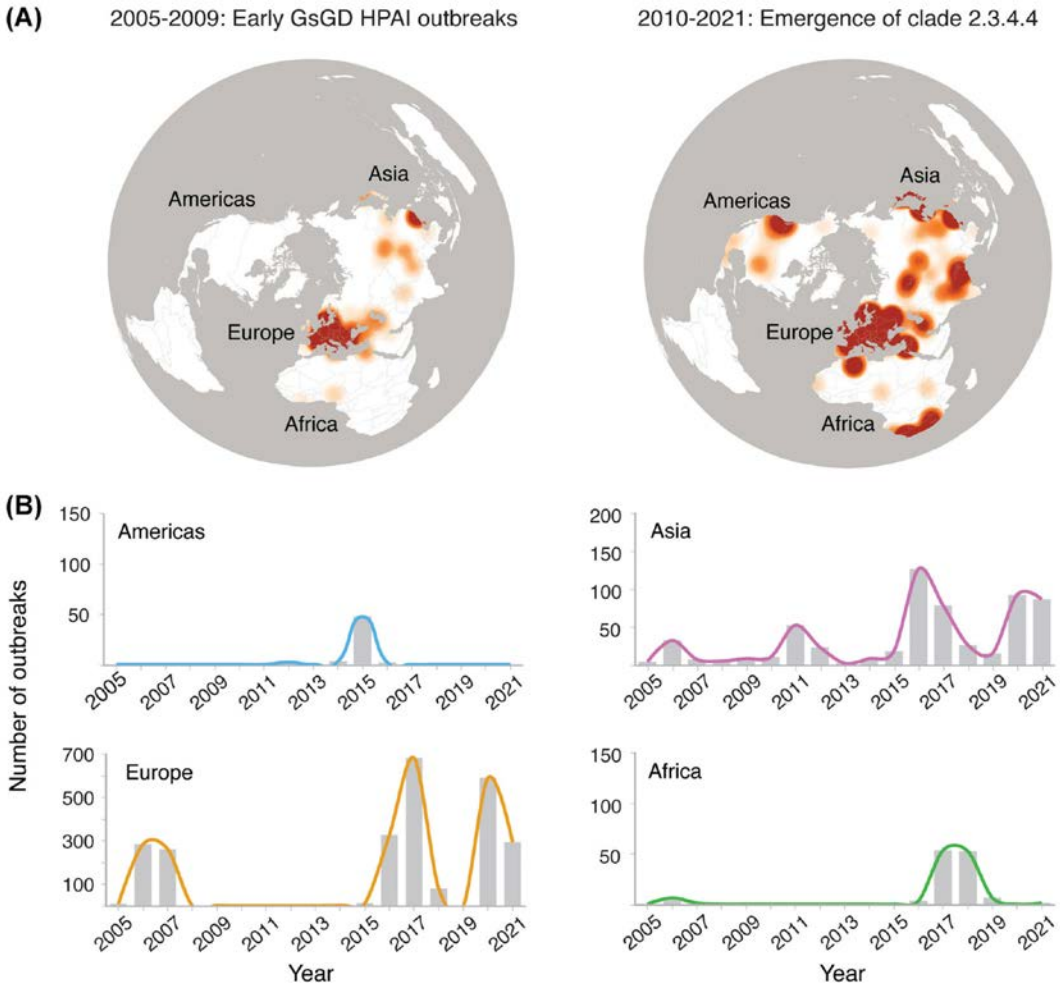
Figure 7 Occurrence of outbreaks of highly pathogenic avian influenza (HPAI) by world region and frequency. Source: Ramey et al., 2022.[137]



LPAI Avian Influenza Subtype Summaries

A(H7N9)

Asian lineage A(H7N9) has a tropism for human and avian cellular receptors (human type α2,6-linked sialic acid and avian-type α2,3-linked sialic acid), thereby causing widespread waves of illness in birds and significant case counts in humans, with an ~39% mortality rate in birds.[146,152]

Identified in birds in 2013, the A(H7N9) 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.[159,160] China experienced six epidemic waves of A(H7N9) in poultry from 2013 to the present, despite aggressive vaccination and culling campaigns in birds.[147]

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.[161]

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Before 2013, Asian lineage A(H7) viruses primarily caused conjunctivitis in humans. With mutations acquired during avian outbreaks between 2013–2017, the A(H7) strain caused 1,568 human infections and 616 deaths in 3 countries. Since 2017, only 3 human cases have been reported.[162]

Influenza Risk Assessment Tool (IRAT)

The Influenza Risk Assessment Tool (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.[109,110]

Four A(H7N9) strains, both Asian and North American lineages, were evaluated using the CDC IRAT.[109] The findings are displayed in Table 2.

A(H7N2)

In 2003, a human case of A(H7N2) was reported in New York. The case had no known poultry exposure.[163]

In 2007, a cluster of human cases was identified in people who had been exposed to infected poultry at a public market in the United Kingdom. Limited person-to-person spread of conjunctivitis was reported.[164]

While not related to an avian exposure, a case of avian-like A(H7N2) was identified in a person who had been exposed to infected cats in an animal shelter in 2016, and later a second case associated with this event was found by serologic testing.[165] 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).[156,166] The outbreak in British Columbia affected approximately 600 commercial poultry farms, resulting in the depopulation of 19 million birds.[166] 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).[166]

A(H6N1)

A(H6N1) is one of the most common avian influenza viruses found 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.[167]

A(H9N2)

The most widely circulating LPAI in the world, the A(H9N2) 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 the 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 poultry in the United States and Europe until the early 1990s.

Table 2 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 Tool[109]

Influenza Strain	Date	Potential Emergence	Potential Impact	Summary Score
H7N9 [A/chicken/Tennessee/17-007431-3/2017]	2017	3.1	3.5	Low
N7N9 [A/chicken/Tennessee /17-007147-2/2017]	2017	2.8	3.5	Low
N7N9 [A/Hong Kong/125/2017]	2017	6.5	7.5	Moderate-high
N7N9 [A/Shanghai/02/2013]	2016	6.4	7.2	Moderate-high

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Since then, the strain has become endemic in domestic poultry in Asia, the Middle East, and Africa.[168] A(H9N2) viruses are often found co-circulating 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.[168] A(H9N2) is believed to have supplied the non-HA and non-NA genes comprising the A(H7N9) LPAI virus that started waves of human and animal infection in China in 2013.[16,160] The virus is split into 2 broad branches: the Eurasian and American lineages.

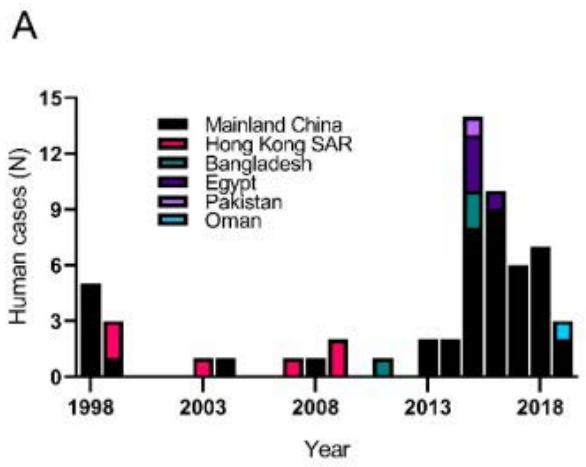
A(H9N2) can infect multiple species including minor poultry species (e.g., quail and pheasants), swine, canine, ferrets, pikas, and bats.[121,169-173]

Early human infections prior to 1998 were asymptomatic and detected only through serologic surveillance.[174,175] As of 2019, 59 human infections and 1 death were reported, with the majority of cases occurring since 2015 (Figure 8). Cases have been concentrated in children younger than 9 years.[168] Two A(H9N2) strains have been assessed using the CDC IRAT: one from Bangladesh in 2014 and another from Jiangxi-Donghu in 2014. Both strains were designated as "moderate" risk.[110]

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.[176] In 2012, 2 cases were confirmed in abattoir workers who had conjunctivitis and minor respiratory symptoms, though 7 other workers exhibited symptoms of illness and did not test positive.[177] Outbreaks were also reported in harbor seals in 2015.[178]

Figure 8 Human cases of A(H9N2), 1998–2019.
Source: Peacock et al., 2019.[168]



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 cases likely acquired infection.[179] 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.[127,141,180] This strain was evaluated using the IRAT and determined to be of "moderate" risk.[110]

HPAI Avian Influenza Subtype Summaries

A(H5N1)

Avian

A(H5N1) was not noted to be a threat to animal or human health until the 1996 emergence of the Gs/GD-lineage in Hong Kong in birds. The first human infection with A(H5N1) was identified less than a year later.[99,181] 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.[99]

The Gs/GD-lineage A(H5) HPAI rapidly became a major panzootic, the first among HPAI noted for its geographic spread and diversity in the species affected. This strain has been found in a wide range of wild and domestic birds and some mammals including felines, canines, and others.[182,183]

Although the original Hong Kong strain found in 1996 was quickly eradicated in Hong Kong, other A(H5N1) HPAIs persisted, causing sporadic outbreaks between 2001 and 2003.[184,185] In late 2003, nearly

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Figure 9 Cumulative human cases of avian influenza A(H5N1) virus, 2003–2021, Source: WHO, 2021.[189]

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
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**	**862**	**455**

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 fatalities in humans.[186] After 2004, a closely related sublineage of A(H5N1) (clade 2.2) was detected in migratory birds.[187] For years following, related viruses circulated in Russia, the Middle East, Europe, and Africa.[188]

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.[11,125] Nevertheless, A(H5) HPAI continues to cause increasing numbers of outbreaks in wild and domestic birds.[3]

Humans

Since 2003, more than 800 cases of A(H5N1) and more than 400 resultant deaths have been reported in 21 countries (Figure 9).[7,122,181] This virus is particularly virulent in humans, causing severe pneumonia and death in 50% of cases.[68] Nearly 500 cases were reported between 2003 and 2009; though these cases were focused heavily in Asia, some were present in Africa as well.[189] In the past 10 years, the number of human infections with A(H5N1) have declined as other AIV subtypes, such as A(H5N6) and A(H9N2) viruses, have become more prevalent.[189,190] While the World Health Organization (WHO) requires reporting of any novel IAV with the capacity to infect a human, cumulative tracking is only published for A(H5N1); however, WHO publishes Influenza at the Human-Animal Interface case reports of all novel IAVs in humans.[191] ProMed provides near-real-time reporting of cases by countries of origin.[192] ProMed reports may not be comprehensive as case reporting is passive and not required. 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.[87,193]

The HPAI A(H5N1) virus affects children and adults; not all human cases have included documented exposure to birds, though 90% of those that did not were in clusters of family members.[54] The median age of infected individuals through 2013 was 18

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years, with 89% younger than 40 years.[26] The overall mortality rate in symptomatic, laboratory-confirmed cases was approximately 50% (Figure 9).[181] Seroprevalence studies suggest that the overall risk of transmission from birds to humans is low, except for those people with prolonged, unprotected exposure to known infected birds.[26]

Three A(H5N1) viruses have been evaluated using the CDC IRAT: A(H5N1) clade 1 Vietnam virus in 2011 rated as "moderate" risk, an A(H5N1) Washington virus in 2015 rated as "low-moderate" risk, and an A(H5N1) clade 2.3.4.4b American wigeon virus in 2022 rated as "moderate" risk.[110]

Additional information about recent AIV infections in humans is located in the Surveillance and Epidemiology section of this guide.

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.[134] Outbreaks of A(H5N2) emerged in France in 2003 and South Africa in 2004 while recurring outbreaks took hold in Asia.[16,153] Between 2012 and 2019, the number of outbreaks and cases grew substantially among poultry to a peak of more than 1 million cases in 2015, mainly in Asia; slightly surging again between 2017 and 2019.[3]

An HPAI A(H5N2) outbreak, which also involved H7N1, was identified in ostriches in South Africa in 2011–2012. Serologic surveys of people with known interactions with sick ostriches revealed 3 A(H5N2) positive cases during a 2-year period. The survey included testing for H7N1, which found 12 people who were seropositive for the virus.[108]

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.[69,130,194] 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.[105,130,195] Wild birds tested along the Pacific flyway were found to be positive for A(H5N2) and A(H5N8) viruses.[129,196] 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.[194,197] This virus, A(H5N2) A/Northernpintail/Washington, was evaluated using the CDC IRAT and determined to be "low-moderate" risk.[110]

Additional details on the H5N2 in North America are located later 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.[198,199] One study confirmed the presence of A(H5N6) (along with A(H7N9) and A(H9N2)) in air samples in the affected markets.[121] The 2013 Eurasian lineage HPAI A(H5N6) virus was a reassortant of A(H5N2) and A(H6N6).[198]

In 2017, A(H5N6) was identified in 3 dead cats in China proximal to outbreak-affected poultry flocks.[200] In 2020, an outbreak was reported in migratory swans in China as the strain continued to circulate in chickens and ducks.[201]

In 2016, a CDC IRAT of HPAI A(H5N6) determined that the virus posed a "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.[110] Of the 51 cases reported globally since 2014, 25 occurred in 2021. Most infected people had been exposed to infected birds before becoming ill.[202]

A(H5N8)

Outbreaks of A(H5N8) have been reported in birds since 1980.[203] However, in 2010, a novel reassortant HPAI A(H5N8) subclade 2.3.4.4b virus, evolved from the A(H5N1) clade 2.3.4, was detected in China in domestic ducks at a live bird market.[106,157,204] The virus remained in China until 2014, when outbreaks were detected first in turkeys in South Korea and later in turkeys in Germany toward the end of that year.[205] 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.[206-208]

A detailed account of the progression of A(H5N8) activity was provided by He et al.[106] in 2021:

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In early 2020, outbreaks of clade 2.3.4.4b viruses mainly occurred in Europe.[209] 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 Japan[209-213]; 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.[201] 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.[209] Recent infections have been reported in seals, swans, and penguins.[213-215] 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.[216]

In 2020, an outbreak of A(H5N8) in Russia was confirmed when approximately 100,000 birds died in December.[203,217]. 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."[110]

A(H7N3)

British Columbia experienced an outbreak of LPAI and HPAI A(H7N3) viruses in 2004.[166] The outbreak in British Columbia affected about 600 commercial poultry farms, resulting in the depopulation of 19 million birds.[166]

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.[3]

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.[218]

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.[119]

A(H7N4)

The A(H7N4) 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.[3,219] A 2-year surveillance along the East Asian-Australasian flyway confirmed the presence of A(H7N4) in migratory birds.[220]

The first and only human case of A(H7N4) was identified in 2018 in a Chinese woman who had been exposed to poultry in a live bird market.[221]

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.[222] In 1996, another human case of A(H7N7) conjunctivitis was identified in England in a woman who regularly interacted with feral ducks.[117]

In 1979, a mass mortality of more than 400 harbor seals was reported in Massachusetts, attributed to A(H7N7).[223]

In 2003, an A(H7N7) outbreak in the Netherlands resulted in 453 reports of health complaints among 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).[224]

In 2013, an outbreak of A(H7N7) was reported in Italy, resulting in the depopulation of more than 1 million birds. Three farm workers had laboratory-confirmed cases of conjunctivitis caused by exposure to infected birds.[165,225]

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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).[226-228]

A(H7N9)

North American lineage

The LPAI A(H7N9) virus strain was first identified in the United States in 2017. Domestic poultry flocks infected with the LPAI A(H7N9) virus were identified in Tennessee, Georgia, Alabama, and Kentucky.[1] Exposure to wild birds was not confirmed by way of testing birds nearby; however, genetic sequencing indicated 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.[147] 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.[159,175] Human infection was again reported in China in 2018.[229]

The A(H9N2) virus has been globally widespread among poultry for the past 2 decades.[168] Multiple outbreaks among swine have been reported as well as infections in mink and bats.[159,230] Several genetic studies suggest that internal genes for A(H5N6) and A(H3N2) viruses of feline and canine came from A(H9N2) viruses.[171,231]

The A(H9N2) virus is hyperendemic in several countries and poses a threat to human health and the global poultry industry.[168] Recent surges in human cases support this threat. The CDC IRAT for the G1 lineage A(H9N2) in 2014 was rated as "moderate" risk, as was the assessment of the Y280 lineage in 2019.[110]

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.[232]

A(H10N3)

The first human case of A(H10N3) was reported by China in 2021. The individual had no clear contact with poultry, and presence of the virus was not confirmed in the local surroundings or nearby poultry.[233]

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.[179,234] 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.[127]

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.[176]

Major Outbreaks of HPAI (and HPAI + LPAI) of the 21st Century Through 2019

In 1996, the H5 Goose/Guangdong lineage emerged in China, resulting in widespread and significant morbidity and mortality in domestic poultry.[26,136,149] The viruses of this lineage were limited to China for the first 7 years, then spread to 8 other countries in Asia by 2004, to Europe in 2005, and to Africa in 2006.[151] Between 2005 and 2019, HPAI H5 viruses resulted in the death and culling of more than 246 million poultry across at least 76 countries. Before 2020, the most significant outbreaks occurred in 2006 and 2016. HPAI spread among birds is highest in China and other countries in Asia from October to a peak in February.[235,236]

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Detailed descriptions of outbreaks occurring in 2020–2022 are provided in this section of the document: Highly Pathogenic Avian Influenza Key Events—International 2020–2023.

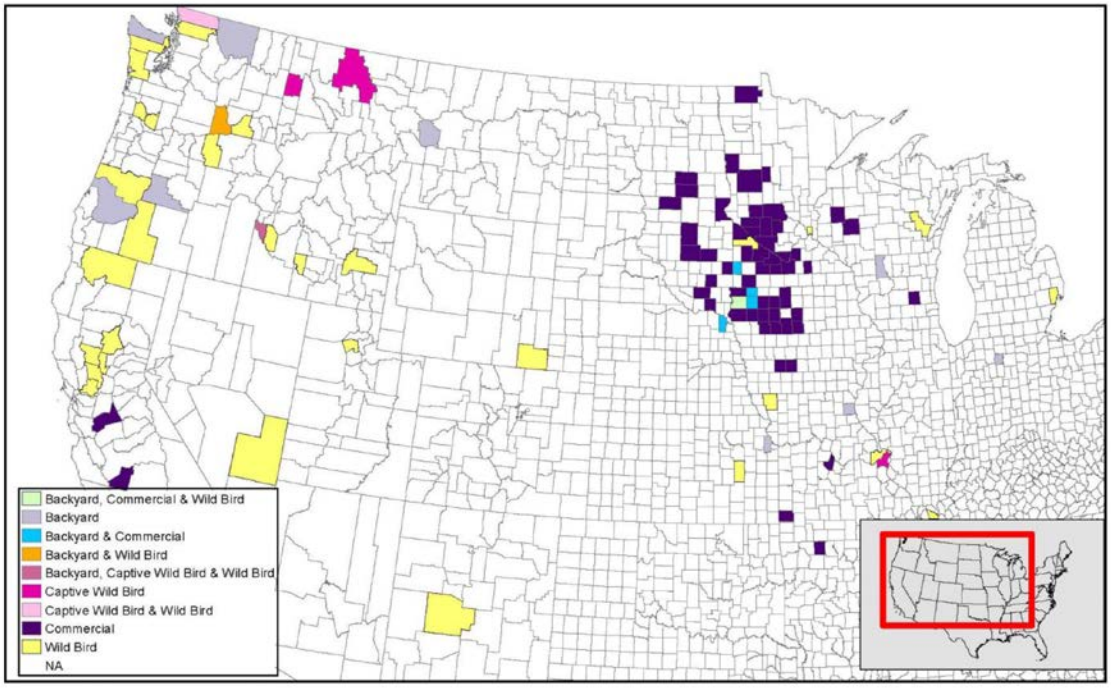
HPAI A(H5Nx) Outbreaks in the United States, Multiple States, 2014–2015

The first appearance of HPAI A(H5N2) clade 2.3.4.4 in North America occurred in 2014. Identified first in Canada and then shortly after in the western and central United States, the event sustained for a little over a year. This event was also notable because the A(H5N2) virus was a reassortment of low pathogenic North American AIV with a Eurasian HPAI A(H5N8) strain.[130,194] The 2014–2015 outbreak affected wild and commercial birds, primarily chickens and turkeys, and resulted in the culling of nearly 50 million birds.[195] The event cost the poultry industry more than $3 billion.[105,130,207,130,194]

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.[68,130,194] 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 as well as North American wild bird lineage neuraminidase (NA) and PB1 genes.[130,194]

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).[18] 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 10).[237]

Figure 10 Highly pathogenic avian influenza virus infections in all birds as of August 31, 2015, United States. Source: USDA APHIS, 2016.[161]



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

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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 the 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.[105]

Outbreaks affecting wild birds and domestic poultry continued in Asia and Europe, and occasionally in Africa after 2015. 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.[214,215,238] As of September 2023, HPAI has not been reported in Australia.[239,240]

Smith et al.[157] provide additional detail on the nomenclature and evolution of A(H5) clades from 2005 to 2012. See the World Organisation for Animal Health Information System for a complete list of avian A(H5) outbreaks from 2005–2021.

HPAI and LPAI Outbreaks in the United States, 2016–2020

This section briefly describes outbreaks of HPAI and LPAI in the United States between 2016 and 2020. These outbreaks do not support undetected circulation in the country, but rather separate emergences of HPAI and LPAI.

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 and displayed 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.[226]

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. Testing confirmed the strain was of the North American lineage and was not related to the Asian A(H7N9) HPAI virus. Lateral spread to multiple farms occurred, and additional farms were identified with broilers infected with HPAI A(H7N9). LPAI was also detected in this outbreak and was potentially co-circulating with HPAI. The outbreak rapidly spread to other farms with different production types and in additional states.[161]

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 in one farm in North Carolina and HPAI in one farm in North Carolina and one farm in South Carolina. No birds were sent to slaughter before testing and detection of AIV, thus limiting potential exposure in production processing.[241]

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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.[23] Outbreaks in swine and subsequent transmission to people occur most often in the 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).[52] Influenza A is endemic in swine populations in Asia, Europe, and North and South America.[242]

Classical swine influenza A(cH1N1) viruses were circulating in North American swine as early as 1930 but were not confirmed in European pigs until 1976.[29,37] A shipment of pigs from the United States to Italy is believed to have resulted in the introduction of SIV to Europe.[243] A few years later, the A(cH1N1) virus was replaced in Europe with a new avian-origin influenza A(H1N1) virus.[78,79,244]

In the United States, A(cH1N1) continued to circulate without influence until 1998, when a triple reassortment event occurred.[29] Double reassortant swine viruses are defined as receiving genetic material from any 2 species infected with influenza, while triple reassortant (tr) viruses contain genetic material from 3 species. In the rare situations in which this 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).[245]

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.[246,247] The incidence of human infection with SIV increased after the emergence of A(trH1N1) in 1998. Between 1998 and 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 before illness onset.[248]

It is important to note that evolution of A(H1N1) viruses over the past 100 years has involved various strains in people and swine (Figure 11).[83,249] 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.[31,78] 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.[29,37] In 1977, an avian-origin A(H1N1) strain reemerged in Russia, causing an epidemic in people. There was an overlap with changes in swine influenza in Europe during the same period, as an avian-origin A(H1N1) virus also emerged in pigs.[78,79,244] In 2009, the A(H1N1)pdm09 strain resulted in a pandemic, and the strain was different from A(cH1N1) and human seasonal A(H1N1).[37]

Swine are often labeled as mixing vessels because they have both mammalian α2,6 and avian α2,3 receptors for IAVs in their tracheal epithelium.[29,52] With a global population of approximately 677 million pigs, these animals have the potential to make significant contributions to influenza virus evolution and transmission; globally, nearly 60% of swine are located in China.[250] Any country, including China, with significant swine populations and proximity to poultry and humans has an increased chance for novel swine strains 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).[115,251] Influenza viruses readily spread from humans to swine, perhaps more frequently than the reverse. Even in the 1918 pandemic and

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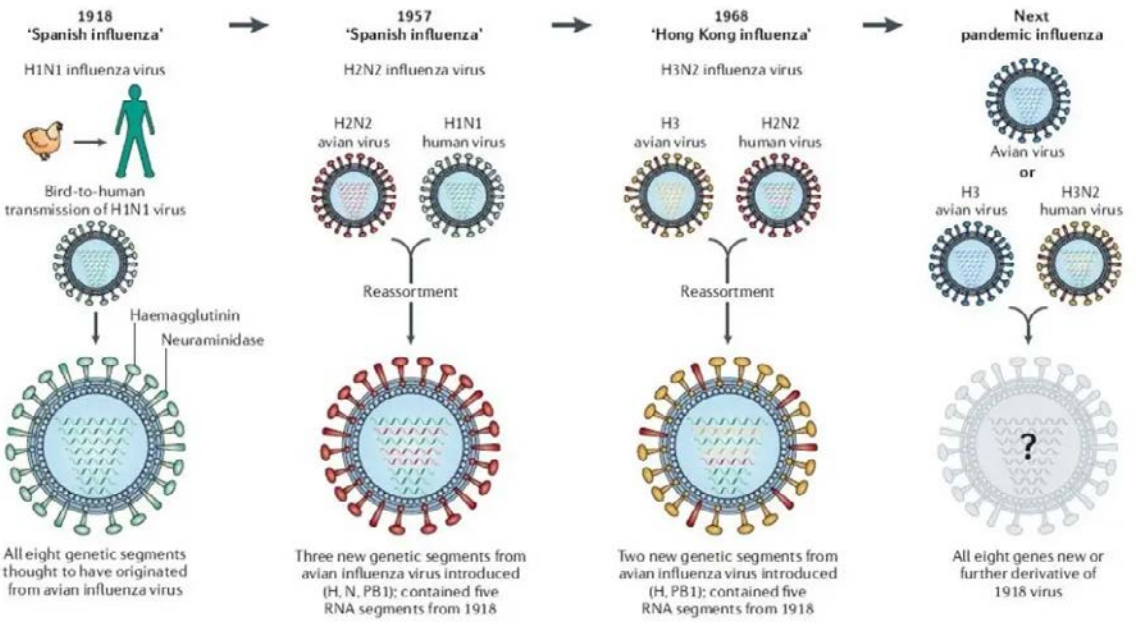
Figure 11 A(H1N1) viruses in avian, swine, and humans, 1918–2009. Source: Nursing and Health, 2014



the A(H1N1)pdm09 pandemic, pig outbreaks temporally followed human outbreaks.[32,78]

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) part of porcine respiratory complex acting with *Mycoplasma hyopneumoniae* and other bacterial pathogens of pneumonia; or 3) no clinical signs of illness.[23,26,29]

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).[75,88] Genetic characterization and phylogenic analysis suggest that A(H1N1)pdm09 was circulating in swine up to 1 to 2 years before its appearance in people.[37,252] In addition, low genetic diversity suggests that the introduction to humans was a single event or a series of events with a similar virus.[37] 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.[26] However, many precursor events in the United States evidenced increasing risk of interspecies transmission of influenza between swine and people.[248]

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 12).[37]

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.[88] The remaining 2 genes, NA and M, were closely related to the 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.[88]

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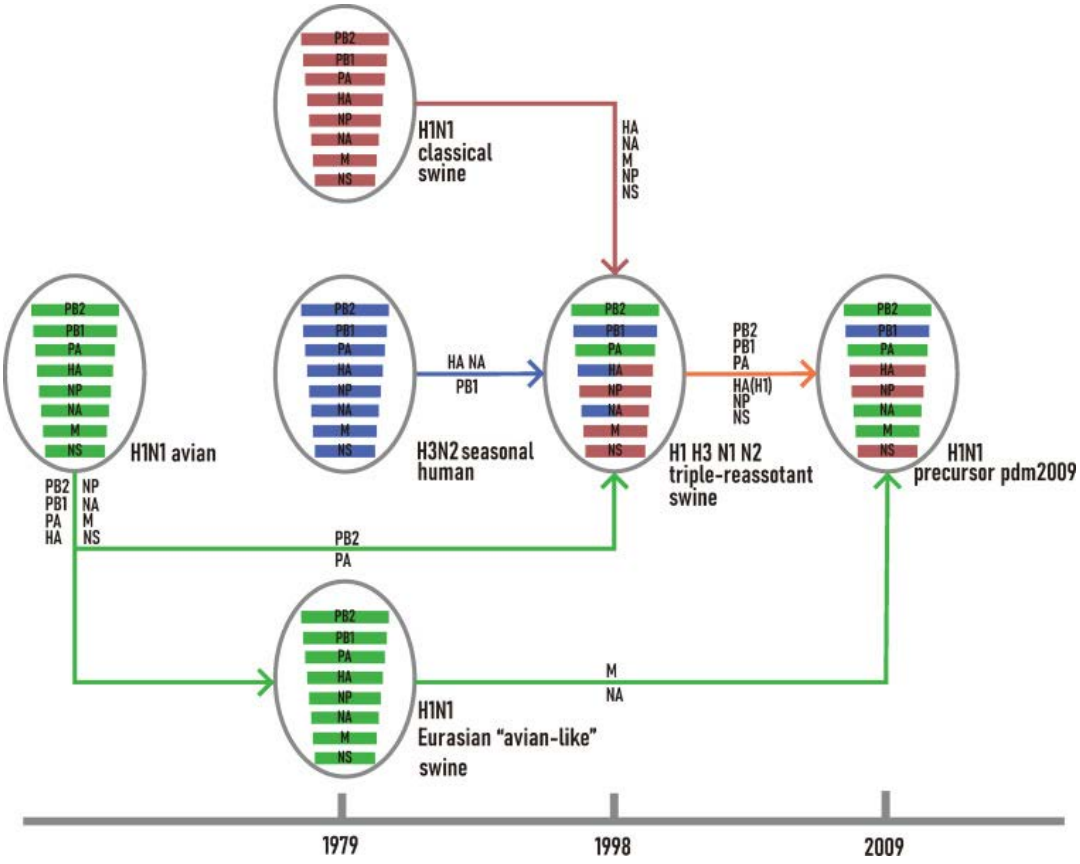
Figure 12 Comparison of human A(H1N1) cases of influenza from triple reassortant swine virus to human cases of A(H1N1)pdm09 influenza. Source: Gao, F., 2020.[6]



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

trH1N1, trH1N2, trH3N2

The swine triple reassortant viruses trH1N1, trH1N2, and trH3N2 are the main influenza viruses circulating among pigs in recent years.[67]

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.[35,253] The 1998 reassortment was the result of humans infecting pigs.[23] Additional reassorting occurred that resulted in new genotypes of A(H1N1) and A(H1N2) retaining the triple reassortant internal genes.[254] These strains represent almost 50% of circulating strains in swine in the United States.[255]

A(H1N2)

The A(H1N2) 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.[256]

A(H2N2)

A(H2N2) circulates in swine and birds but has not been identified in humans in more than 40 years. This strain became a dominant seasonal strain after the pandemic in 1957 but then dissipated in 1967.[257]

A(H3N2)

SIV A(H3N2) is distinct from the human seasonal A(H3N2) virus in that it normally circulates in pigs and causes sporadic human infections.[14] 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)

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more transmissible to humans. Although only 11 human cases of novel influenza from swine were reported between 1998–2009, 12 human cases were confirmed in 2011 alone, followed by a record 300 cases in 2012. The majority of these events were attributed to an H3N2v virus, as displayed in Figure 13.

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.[255,259-263]

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 and then from 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.[253] 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.[87] Swine have cellular receptors for avian and mammalian influenza viruses, and avian A(H5) infections in pigs have occurred.[29,52]

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.[264]

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.

Figure 13 U.S. novel influenza A infections in humans. Source: CDC Outbreaks, 2024.[258]

	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	2022-23	2023-24	Total
Influenza A H1N1v	0	2	2	0	3	1	0	1	1	0	8	0	0	0	18
Influenza A H1N2v	0	4	0	0	0	3	4	14	0	0	4	6	2	1	38
Influenza A H3N2v	7	315	20	3	3	19	61	2	0	1	2	5	1	0	439
Influenza A H7N2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Influenza A H1v	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Influenza A H3v	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Influenza A H5N1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2
Total	7	321	22	3	6	23	66	17	1	1	14	13	4	2	500

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Influenza Viruses in Equine

Overview

Equine influenza virus (EIV) is a highly contagious common infection of horses, with historical documentation of incidences dating back centuries.[265] Often overlooked outside of equine communities, outbreaks have disrupted horse racing and the show industry, as well as impacted 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.[266] Periodic, significant outbreaks also occur in countries like Mongolia in nomadic horse herds, where outbreaks affect associated economies.[267]

Equine influenza causes acute symptoms of infection including dry cough, lethargy, fever, nasal charge, and anorexia that typically resolve within 2 weeks[268] EIV is believed to have originated from avian influenza viruses. EIV can infect all equids, wild and domestic, including donkeys.[269,270] EIV can spill over to dogs, cats, swine, and likely many other mammals. Transmission from horses to humans is possible.[271] Humans can also infect horses with human influenza, though the subsequent infection in horses is usually asymptomatic.[272] Elevated antibodies to EIV have been detected in humans during multiple EIV outbreaks.[266]

A(H7N7)

A(H7N7) was first identified in horses in Europe in 1956 and was last identified in the 1970s, though serologic tests suggest that circulation ended in the 1990s.[81,273]

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 14).[274-278] 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.[279]

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 horse from Japan whose illness was missed at an Australian quarantine station. The estimated cost of that outbreak exceeded $1 billion.[107] Another significant, international outbreak started in Chile in 2011–2012 and spread to numerous countries.[268] In 2022, an outbreak among wild horses and burros was reported in Colorado. The horses were rescued during a wildfire the year prior, and the outbreak occurred at the holding facility where the horses were housed.[280]

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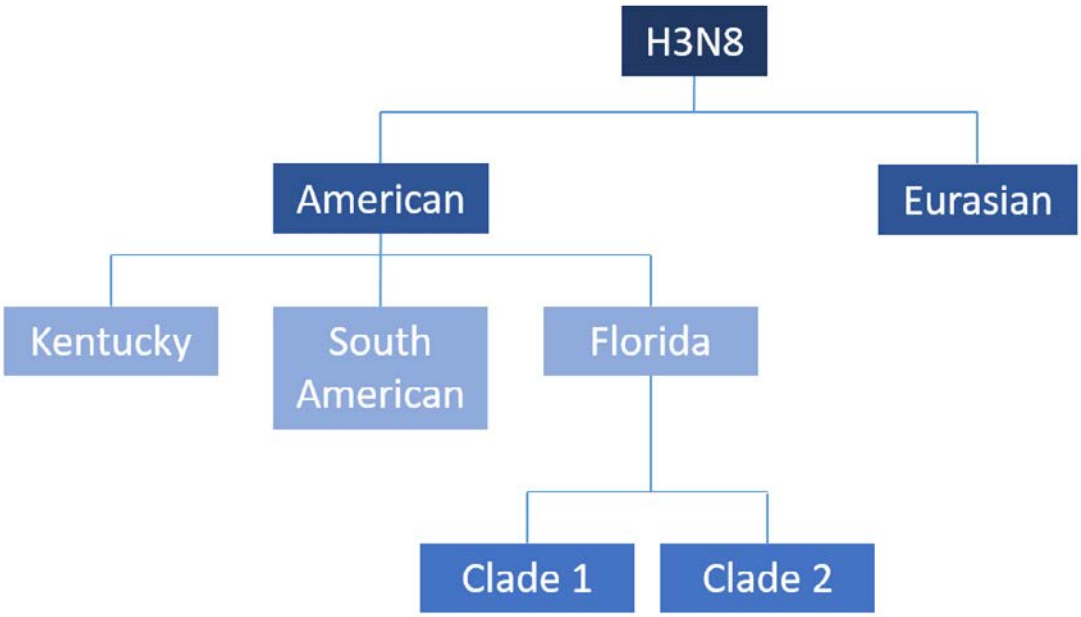
Figure 14 Equine influenza A(H3N8) virus American and Eurasian sub-lineages, University of California, Davis, 2019.[81]



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Influenza Viruses in Canine & Feline

Overview

Influenza A virus (IAV) is spread between and among dogs and cats, and occasionally between the 2 species through respiratory droplets. As shown in Figure 15, 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.[87] Feline infections from avian influenza viruses (AIVs) include low pathogenic avian influenza (LPAI) A(H7N2) and highly pathogenic avian influenza (HPAI) A(H5N1). The A(H1N1) pdm09 strain infected both felines and canines in 2009.[281]

Both dogs and cats contain receptors for both mammalian- and avian-type IAVs (mammalian α2,6-linked sialic acid and avian α2,3-linked sialic acid), making them a potentially important link in interspecies transmission of influenza viruses.[171,282] Multiple studies have shown 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.[281,283] 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.[284] 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.[171,285,286] Despite the known presence of mammalian and avian influenza receptors in cats,

Figure 15. Overview of major influenza A virus infections reported in dogs and cats. Source: Borland et al., 2020.[281]

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)

[a]CIV, 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.
[b]Refers to endemic subtype in canine population.
[c]Severity was defined based one the following criteria: + mild respiratory symptoms; ++ severe respiratory symptoms; +++ systemic infection.
[d]Intraspecies transmissibilty 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.
[e]Reverse Zoonosis refers to an influenza subtype that can be transmitted from humans to companion animals.

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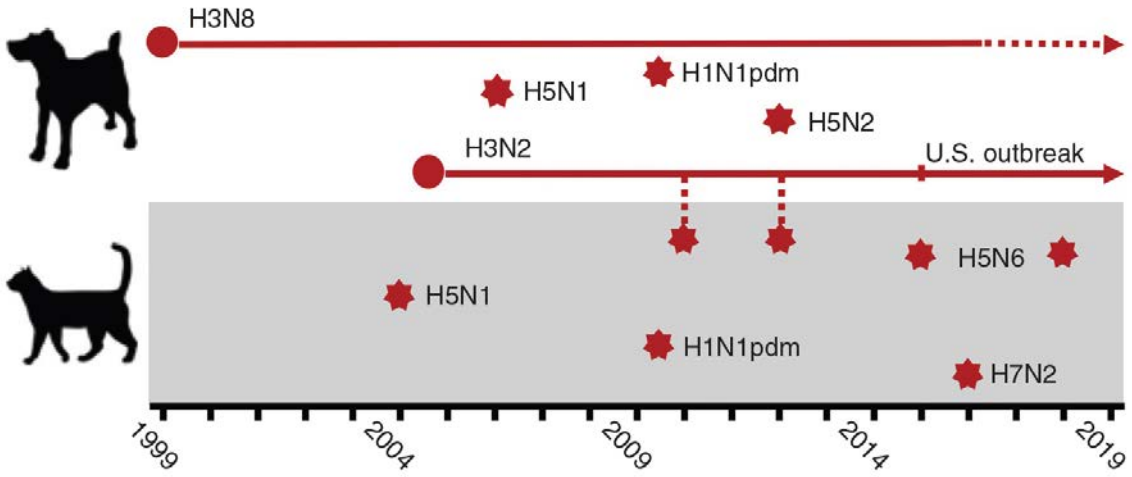
Figure 16 Canine and feline influenza A virus evolution 1999–2019. Source: Wasik et al., 2021.[283]



the species was not known to be one in which reassortment of IAV took place until a detection event occurred in China in 2017.[231]

The following is a description of Figure 16 from Wasik et al.[283] in 2021.

> *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.*

Outbreaks in the United States

Canine influenza A(H3N8) was first identified in the United States in 2004. The outbreak started in racing greyhounds in Florida and spread to 11 states over the following 2 years.[287,288] Sporadic outbreaks of A(H3N8) continued through 2019, after which the virus has not been detected.[289] Canine influenza A(H3N2) was introduced to the United States in 2015. Sporadic outbreaks continue to present day.[290-293] A(H3N2) may become endemic in the United States due to sustained activity in multiple states.[294-296] Vaccination for canine flu is available for both A(H3N8) and A(H3N2) but is not routine.[290] In addition, the United States does not have stringent laws for the importation of dogs, which can result in the continuous reintroduction of canine influenza.[294]

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.[288] 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.[287,288] Around the time of the 2004 Florida outbreak, other outbreaks were noted in dogs in Australia, the United Kingdom, and South Korea.[171,297,298]

At present, there is no evidence of transmission of A(H3N8) from canines to humans.[299] CIV A(H3N8) circulated until around 2019 in Colorado and the northeastern United States, mainly in animal shelters and kennels with a high turnover of animals.[22,288] The lack of recent activity suggests possible extinction of this virus.[289]

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A(H3N2)

CIV A(H3N2) appears to have originated in birds, then infected dogs, and now spreads between dogs.[22] 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, the CIV A(H3N2) virus was confirmed in dogs in the United States. Following introduction of the virus to the United States, an outbreak in Chicago in 2016 infecting more than 1,000 dogs resulted in sustained low-level transmission despite shelter control efforts.[300] Although the original US outbreak died out, the virus is continually reintroduced by dogs imported from Asian countries, where the disease is endemic.[301,302] Two outbreaks in shelter dogs—one occurring in 2017 and the other in 2021—have been reported in Los Angeles County, California.[291,303]

Other Strains

Between 2014–2015, swine influenza virus reassortant A(H1N1), A(H1N2), and A(H3N2) infections in dogs were reported in China.[281]

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.[304] 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 later.[283,304]

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.[212,305]

A(H5N1)

The HPAI 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.[306,307,] Studies involving field serosurveys show that the prevalence of HPAI 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 cats' consumption of infected birds.[306,308]

A(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. Between 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.[283] Feline infections may have been acquired from interactions between domestic cats and wild birds, whether through cats feeding on infected birds or by other direct contact.[200]

A(H7N2)

A feline outbreak in a New York City animal shelter in 2016 was attributed to an LPAI A(H7N2) virus.[309,310] Two human infections were confirmed:1 case in a veterinarian who displayed mild symptoms and a second case, confirmed retrospectively, in which no symptoms were reported. These were the first known human infections with A(H7N2).[165,310]

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.[212]

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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 2009 when influenza virus-infected bats were identified in Guatemala. This discovery was the result of a 2-year surveillance study to assess influenza virus prevalence in Guatemalan fruit bats.[311]

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.[311,312] 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.[19,312] These discoveries indicated 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.[19,313] 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.[19]

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.[314-316]

Additional Resources

Bat Influenza (Flu) | Seasonal Influenza (Flu) | CDC

Bat Influenza Viruses: Current Status and Perspective (mdpi.com) [317]

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Influenza in Other Animals

Sea Mammals

Seals and other pinnipeds are susceptible to influenza A virus infection, which likely results from onshore interactions with wild birds[318]. Notable outbreaks among harbor seals include A(H7N7) in Cape Cod, Massachusetts, in 1980, A(H3N8) in the northeastern United States in 2011, and A(H10N7) in Denmark and Sweden in 2014. Seals experience pneumonia from influenza virus infections, which can cause significant mortality. Seals may also acquire influenza B virus infections from humans.[17,178,223,319]

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.[16] 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 pathogenic avian influenza (LPAI) A(H7N1) virus. Extensive serologic testing was conducted in nearly 400 people involved in outbreak mitigation in 2011 and 2012. Human infection with the HPAI A(H5N2) virus from 2011 was confirmed in only 3 individuals, whereas serologic evidence of LPAI A(H7N1) virus infection from 2012 was present in 4 ostrich abattoir workers and 4 veterinarians. 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.[108]

Pandas

A single case of A(H1N1)pdm09 was detected in an asymptomatic panda in Hong Kong in November 2018.[24]

Penguins

AIV A(H11N2) was detected in Adelie penguins in Antarctica in 2013. Genetic examination revealed diverse origins of the virus, though the majority of segments were from North American lineage viruses with neuraminidase (NA) genes derived from Eurasian lineages.[320] 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 A(H11) viruses already present on the continent.[321] 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.[214] These discoveries highlighted the persistence of influenza viruses, reassortment between lineages in Antarctica, and the potential for a devastating introduction of HPAI viruses to the Antarctic penguin population.[320]

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.[322] Research investigating the role of wild or domesticated ferrets in influenza transmission is sparse.

Other Mammals

An international outbreak of HPAI A(H5N1) clade 2.3.4.4b virus, which began in 2021, subsequently resulted in the infection of multiple new species.[434,435] For more information, see the following section: *Impact on Mammals – International and United States*.

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Outbreak in Cattle and Other Animals

The USDA APHIS reported an outbreak of HPAI A(H5N1) clade 2.3.4.4b in multiple U.S. states in livestock, mainly dairy cattle. Wild migratory birds were believed to be the source of the outbreak in cattle and sequencing of the virus in cattle indicates initial infections might have occurred in December 2023. Detections in domestic poultry increased over the previous year into spring 2024 coinciding with the outbreak in cattle. At the time of writing, one human case, detailed in a later section of this document, was reported in connection to this outbreak. Transmission between cows is believed to be occurring through contaminated surfaces and possibly milk. Additional animals affected by this outbreak include goats and felines suggesting the virus has better adapted to infect mammals.

Detailed information on this outbreak is located here:
Highly Pathogenic Avian Influenza (HPAI) Detections in Livestock | Animal and Plant Health Inspection Service (usda.gov)

CDC resources on this outbreak and the human case are located here:
Current H5N1 Bird Flu Situation in Dairy Cows | Avian Influenza (Flu) (cdc.gov)

Additional Resources

For a list of mammals currently affected by the U.S. HPAI A(H5N1) outbreak, click on USDA APHIS | 2022-2023 Detections of Highly Pathogenic Avian Influenza in Mammals. For a cumulative list of mammals affected by influenza, see WAHIS: World Animal Health Information System on the WOAH website.

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Surveillance, Epidemiology, and Prevention and 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. This section also contains comprehensive information on the HPAI A(H5Nx) global outbreak.

US and International Human and Animal Surveillance: Quick Reference

Table 3 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.[125] 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. In addition to the surveillance site links below, many state animal health and public health agencies publish state-level reports with more granular information.

Human Influenza Surveillance and Epidemiology

Human (Seasonal) Influenza Surveillance in the United States

According to the Centers for Disease Control and Prevention (CDC),[323]

> *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 the following:

- **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 healthcare 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.

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Table 3 Surveillance report references for human, avian, and swine influenza viruses, by U.S. 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)*	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†	USDA APHIS Quarterly SIV Reports	
Avian (poultry)	Highly Pathogenic Avian Influenza	WOAH-WAHIS
Avian (wild–terrestrial and aquatic)	WHISPers (usgs.gov) Avian Influenza And Wild Birds Highly pathogenic avian influenza	WOAH-WAHIS
Mammals	USDA APHIS | 2022-2023 Detections of Highly Pathogenic Avian Influenza in Mammals	WOAH-WAHIS
Outbreak reports	Highly pathogenic avian influenza	Disease Outbreak News (who.int) Influenza Research Database The Weekly Epidemiological Record

**"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.*

†Influenza is endemic in swine and not actively surveyed at the international level. 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).

- **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 the severity of seasonal flu. 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 at Overview of Influenza Surveillance in the United States.

These surveillance efforts are intended to detect trends and ascertain broad impact. As such, they represent a subset of the actual impact of influenza activity. The data from these systems are intended to inform public health decisions and produce situational awareness, provide insight to healthcare 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 in the Weekly US Influenza Surveillance Report. Summaries of overall activity and data from each FluView reporting system are included in these weekly reports.

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The CDC Influenza Division has an emergency contact line that is staffed 24/7. This number may be used by public health officials at any time for questions about influenza: CDC Influenza Division: 404-639-3747. Additional contacts include CDC INFO (on website): Contact CDC-INFO; 800-CDC-INFO (800-232-4636); and TTY: 888-232-6348.

State and many local health departments also maintain 24/7 after-hour contact numbers for infectious disease emergencies. Local healthcare providers and other community organizations are encouraged to contact their respective health department first regarding infectious disease concerns. 24/7 contact information for health departments is available at https://www.cste.org/page/EpiOnCall. Health departments will facilitate communication with CDC when appropriate.

Additional contact information is provided in Appendix A.

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. To find state-specific influenza and other respiratory pathogen surveillance, click on the following web page and scroll down: Weekly US Influenza Surveillance Report.

CDC publishes hospitalization data for COVID-19, flu, and respiratory syncytial virus (RSV) on the following site: RESP-NET Interactive Dashboard | CDC. Data are collected from 13 states and represent over 29 million people. These dashboards are refreshed weekly.

Human (Novel) Influenza Surveillance in the United States

Influenza Surveillance and Monitoring of Swine Workers

People who work with swine should be familiar with the symptoms of influenza. Seasonal flu viruses can be transmitted from workers to pigs. Workers who experience symptoms of influenza-like illness (ILI) should notify their supervisor and employer, and be referred to a healthcare provider to determine the need for testing and prescription for antiviral medication if appropriate (ideally within 2 days of symptom onset).[324]

Swine workers with ILI should limit contact with other people and limit travel for at least 24 hours after a fever is gone.

Healthcare providers caring for patients who have ILI and have recent swine exposure should contact their local or state health department for additional influenza specimen testing.[324]

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

Influenza Surveillance and Monitoring of Poultry Workers

Following identification of HPAI-infected birds or mammals, state or local public health officials conduct contact tracing to identify and monitor individuals potentially exposed to the virus without wearing appropriate personal protective equipment (PPE).[325-327] Exposed individuals may include anyone in contact with sick or infected birds, facilities, or farming equipment such as farm workers, persons who routinely visit farm facilities, persons who operate farm equipment, persons who transport animals, persons who process animals, and personnel responding to wild waterfowl die-offs, wild or sick marine animals, or commercial poultry. Any person exposed to HPAI is recommended to be monitored for symptoms of illness for up to 10 days after the exposure. Monitoring includes communication with the exposed individual, asking for the presence of symptoms, and coordination for testing if symptoms appear. CDC may request that jurisdictions report monitored individuals to CDC as part of national surveillance efforts.[326,327] CDC should also be notified of testing performed for a person with a recent HPAI exposure.[14] Persons who are exposed to HPAI are not generally required to quarantine during their monitoring periods.[14,326]

Guidance for public health surveillance of HPAI-exposed individuals is located at Public Health Monitoring Plan for USDA APHIS Responders to Detections of Avian Influenza Virus in Poultry

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The suggested CDC definitions for tracking and reporting human infection with avian influenza are located at Case Definitions for Investigations of Human Infection with Avian Influenza A Viruses in the United States (cdc.gov)

Testing guidance for persons with suspected avian influenza is located at Interim Guidance on Testing, Specimen Collection, and Processing for Patients with Suspected Infection with Novel Influenza A Viruses with the Potential to Cause Severe Disease in Humans | Avian Influenza (Flu) (cdc.gov)

Due to the outbreak of HPAI A(H5N1) in cattle, the CDC has revised interim guidance for the surveillance of persons exposed to HPAI. Guidance includes testing protocols for persons meeting certain epidemiologic, clinical, or public health criteria. Please refer to the following website for the most up-to-date testing and monitoring recommendations for human exposures to HPAI.

Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations | Avian Influenza (Flu) (cdc.gov)

The CDC Influenza Division has an emergency contact line that is staffed 24/7. This number may be used by public health officials at any time for questions about influenza: CDC Influenza Division: 404-639-3747. Additional contacts include CDC INFO (on website): Contact CDC-INFO; 800-CDC-INFO (800-232-4636); and TTY: 888-232-6348.

Local healthcare providers and other community organizations are encouraged to contact their respective health department regarding infectious disease concerns. 24/7 contact information is available at: https://www.cste.org/page/EpiOnCall.

Impact of SARS-CoV-2 on Influenza Surveillance

Many influenza surveillance systems have been expanded and reinforced 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.[323]

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Seasonal Influenza Vaccine Recommendations

CDC provides seasonal vaccine recommendations and clinical guidance for each influenza season on this website: 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 online at Vaccine Effectiveness Studies. The 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 recommendations from the Advisory Council for Immunization Practice. Content is updated frequently and is highly relevant.

International Surveillance of Human (Seasonal) Influenza

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, six WHO Collaborating Centres, four Essential Regulatory Laboratories, and several others.[101]

Laboratory surveillance data are available in real-time on FluNet: FluNet Summary (who.int) and Global Influenza Programme (who.int). These reports include A(H1) and A(H5) human cases.

Summaries and details of human cases of avian influenza virus (AIV) and swine influenza virus (SIV) are provided semi-monthly 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 at 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 the member countries have met the requirements of the 2005 IHR treaty.[328] While surveillance is becoming increasingly robust, numerous gaps exist in countries with inadequate public health surveillance systems.

SARInet is a collaborative between the Pan American Health Organization/WHO and laboratory, healthcare, and other institutions in the Americas conducting surveillance of acute respiratory infections. In recent years, H5 human cases in South America and Cambodia were first reported by SARInet. Surveillance reports are available at ais.paho.org.

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. See 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 United States, 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.[329]

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.[330] 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.[330] Codetection of these pathogens with the A(H1N1)pdm09 virus in humans occurred in 2009; codetection also occurred with SARS-CoV-2 infection.[331-333]

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). NREVSS monitors temporal and geographic patterns of multiple respiratory diseases. Participating U.S. laboratories report weekly aggregate tests and weekly aggregate positive tests. NREVSS enables timely analysis of viral seasons.[330]

Human Non-influenza Respiratory Pathogen—Specific Surveillance

The following list provides 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

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Epidemiology and Transmission Dynamics

Seasonal influenza

Seasonal influenza affects populations in the Southern Hemisphere primarily during the US summer months and then moves to the Northern Hemisphere during the US winter months.[334] 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).[91] After the pandemic in 2009, A(H1N1)pdm09 now circulates as the predominant A(H1) strain along with A(H3N2). The B/Yamagata strain currently circulates much less than B/Victoria and may die out in future seasons.[11]

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.[335] 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.[335] Influenza activity levels for 2021–2022 in comparison to past years are still being assessed.[336] 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 on the following CDC webpage: 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 those in 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.[337]

National FluSight, state, and other forecasts are located at this website: Epidemic Prediction Initiative (cdc.gov). (*Note: forecasting for seasons beyond 2019–2020 may not be available due to the SARS-CoV-2 pandemic*.)

Prevention and Control

Vaccination

Human (seasonal) influenza vaccination is the most effective way to prevent influenza illness. The composition of each annual influenza vaccine used in the United States is determined by CDC. A description of how strains are selected for inclusion into the seasonal influenza vaccine is located at Selecting Viruses for the Seasonal Influenza Vaccine.[63] 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.[63]

More than 144 influenza centers from 114 countries conduct year-round surveillance for influenza viruses by submitting specimens to the WHO Collaborating Centres.[63,109] Twice annually, directors of these 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 up 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.[63] A CDC collection of literature regarding the benefits of influenza vaccination is located at Benefits of Influenza Vaccination.

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 those listed below lower the risk of acquiring and spreading influenza.[338]

- Handwashing
- Frequent cleaning and disinfection of high-touch surfaces
- Covering coughs
- Use of face masks
- Isolating when ill
- Quarantining when exposed (if recommended)

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Most people with influenza illness are contagious 1 day before the onset of illness through 3-4 days after illness onset.[339]

Antiviral treatment may decrease the period of illness and lessen the impact of symptoms if started quickly after the onset of illness. Rapid administration of antiviral medication is recommended for persons at increased risk for serious illness from influenza.[65]

More online information from CDC on antiviral medication is located at Treatment: What You Need to Know

Surveillance for Novel Influenza A Viruses in Humans

Novel Influenza Surveillance in the United States

Novel influenza A virus infections in people became a nationally notifiable disease in the United States 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.[340] Novel influenza A virus strains are detectable using routine laboratory methods, but the determination of their subtype and confirmation of a 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 available from this CDC website: CDC A(H1N1) Flu|Clinical Data Collection Forms and Templates.[340]

To date, events of swine, avian, and avian-origin feline zoonotic influenza virus transmission 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 but may also include avian influenza A(H5N1). Globally, novel virus subtypes may include A(H2), A(H5), A(H7), and A(H9), as well as SIV A(H1) and A(H3).[13,97] A potential weakness of the US surveillance system is its dependency on healthcare 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.[248]

In the United States, 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 (outside of A(H1N1)pdm) occurred in 2012, when 309 human cases of A(H3N2)v (SIV) were identified, including 16 people who were hospitalized and 1 who died.[261,341,342]

CDC reports all novel influenza A virus infections in its weekly national influenza surveillance report, FluView: Reports of Human Infections With Variant Viruses. Figure 17 presents an excerpt from the FluView report on novel influenza A virus in humans.

Infections of AIV in Humans—Prior to 2020

HPAI A(H5) and A(H7) viruses are generally maladapted to humans, but when infection does occur it may be highly lethal.[181] Since 1997, more than 868 cases of A(H5N1) virus infections in humans in 21 countries have been reported, with a case fatality rate of approximately 50% (Figure 18).[122,181,189] The countries with the highest case counts for A(H5N1) include Egypt, Indonesia, Vietnam, China, and Cambodia.[343]

Several AIV strains of the A(H7) virus have caused human infections. LPAI A(H7N3) has caused minor cases of conjunctivitis in 2004 in Canada and in 2012 in Mexico.[166,218] LPAI A(H7N7) infections in humans have been reported sporadically and alongside poultry outbreaks since 1959, and also usually cause conjunctivitis in people.[225] Both LPAI and HPAI A(H7N9) virus infections reported in China caused severe illness, with high case fatality rates of more than 40% among persons who had been hospitalized.[121,142,144-147,159,160,344]

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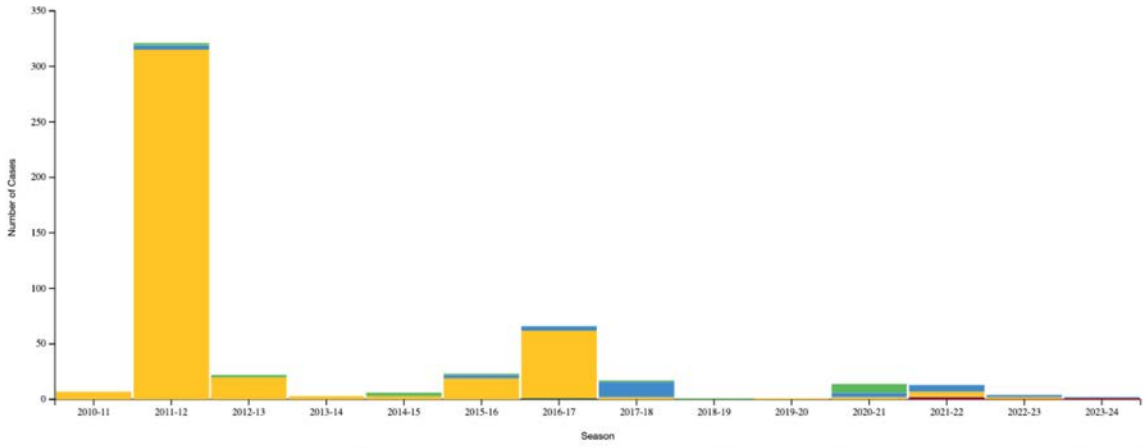
Figure 17 Human novel influenza A virus infections by season and subtype. Source: CDC FluView, 2024.[2]



	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	2022-23	2023-24	Total
Influenza A H1N1v	0	2	2	0	3	1	0	1	1	0	8	0	0	0	18
Influenza A H1N2v	0	4	0	0	0	3	4	14	0	0	4	6	2	1	38
Influenza A H3N2v	7	315	20	3	3	19	61	2	0	1	2	5	1	0	439
Influenza A H7N2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Influenza A H1v	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Influenza A H3v	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Influenza A H5N1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2
Total	7	321	22	3	6	23	66	17	1	1	14	13	4	2	500

The tracking of AIV infections in humans is coordinated by WHO, though the epidemiologic details of each case report depend on what data member countries can provide. WHO provides quasi-monthly reports of AIV human infections with risk assessments by subtype titled "Influenza At The Animal-Human Interface Summary And Assessment."[345] These reports also include human cases of swine (or variant) influenza virus infections. International Health Regulations require the reporting of novel influenza cases in humans as described below:

> *All human infections caused by a new influenza subtype are required to be reported under the International Health Regulations (IHR, 2005). This includes any influenza A virus that has demonstrated the capacity to infect a human and its haemagglutinin gene (or protein) is not a mutated form of those, i.e. A(H1) or A(H3), circulating widely in the human population. Information from these notifications is critical to inform risk assessments for influenza at the human-animal interface.*[346]

WHO reports on novel human AIV and SIV infections[347] can be found at Global Influenza Programme (who.int).

WHO also tracks cumulative counts of AIV A(H5N1) infections in humans[345]: Global Influenza Programme (who.int).

CDC provides detailed case information[343]: Reported Human Infections With Avian Influenza A Viruses.

For a CDC epi curve displaying A(H5N1) human cases internationally from 1997 to the present,[348] click on Past H5N1 Human Infections by Country.

For a detailed chronology of avian flu activity from 1880s forward, click on Highlights in the History of Avian Influenza (bird flu).[349]

Human Cases of Avian Influenza A, International—2021

As of January 8, 2022, 66 AIV cases were 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 before the onset of illness.[350]

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Figure 18 Cumulative number of confirmed human cases† for avian influenza A(H5N1) reported to WHO, 2003-2024.[441]

Country	2003-2009*		2010-2014*		2015-2019*		2020		2021		2022		2023		2024		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	6	1	1	0	0	0	0	0	0	0	0	0	0	0	8	1
Cambodia	9	7	47	30	0	0	0	0	0	0	0	0	6	4	5	1	67	42
Canada	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Chile	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
China	38	25	9	5	6	1	0	0	0	0	1	1	1	0	0	0	55	32
Djibouti	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Ecuador	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Egypt	90	27	120	50	149	43	0	0	0	0	0	0	0	0	0	0	359	120
India	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	1
Indonesia	162	134	35	31	3	3	0	0	0	0	0	0	0	0	0	0	200	168
Iraq	3	2	0	0	0	0	0	0	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	0	0	0	0	0	0	3	2
Myanmar	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Nepal	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
Nigeria	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	1
Spain	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	2	0
Thailand	25	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	4
United Kingdom	0	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0	5	0
United States of America	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	2	0
Viet Nam	112	57	15	7	0	0	0	0	0	0	1	0	0	0	1	1	129	65
Total	**468**	**282**	**233**	**125**	**160**	**48**	**1**	**0**	**2**	**1**	**6**	**1**	**12**	**4**	**7**	**2**	**889**	**463**

*2003-2009, 2010-2014 and 2015-2019 total figures. Breakdowns by year available on subsequent tables.
†This count includes reported detections in asymptomatic individuals. In some cases, the confirmation of infection versus transient contamination of the nasopharynx/oropharynx with virus particles after exposure to infected birds or contaminated environment remains inconclusive. Total number of cases includes number of deaths.
WHO reports only laboratory-confirmed cases. All dates refer to onset of illness.
Source: WHO/GIP, data in HQ as of 3 May 2024.

World Health Organization

As of the start of 2021, only 29 laboratory-confirmed human infections with A(H5N6) had been reported since 2016.[125] In 2021, 30 cases were reported, 12 of which were confirmed to be 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 one case of A(H10N3).[139,350,352] Russia reported several infections with A(H5N8) in humans, along with substantial domestic and wild bird outbreaks along the southwest border with Kazakhstan.[125] 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.[125] India also reported 2 cases of A(H5) in teenagers with distant exposure to birds.[352]

Human Cases of Avian Influenza, International—2022

A total of 55 human cases of avian influenza were reported in WHO human-animal interface reports published in 2022 (Table 5).[346,350,353-359] Due to variability in the timing and completeness of reporting to WHO and within WHO human-animal interface reports, including the absence of symptoms or onset date for some cases, cases counted for 2022 in this reference guide were based on date of publication rather than date of illness onset.

Table 4 Human cases of avian influenza virus by subtype in 2021[351]

	H5N6	H9N2	H5N8	H10N3	H5	Total*
Case Counts	30	21	7	1	7	66

**Case counts may be updated in future reports from the World Health Organization. Cases are counted for the year in which they were reported.*

One report of H3N8 virus infection in a child occurred in China; the child had been exposed to a live poultry market prior to the illness but had no direct contact with poultry (Table 5). Samples taken from the market visited by the child did not confirm the presence of H3N8 virus. While H3N8 viruses are common among domestic and wild birds, this was only the second human case of H3N8 ever reported with the prior case reported in 2021.

Detection of A(H5N1) virus clade 2.3.4.4b—2022

Active surveillance among poultry workers significantly increased in 2022 due to ongoing outbreaks mainly in Europe and the Americas. As a consequence, several detections of H5N1 in humans are being counted as cases with the caveat that transient contamination of the nasopharynx/oropharynx after exposure cannot be ruled out.[318] These include reports from

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Table 5 Human cases of avian influenza virus by subtype in 2022 [346,350,353-359]

	H5	H5N1	H5N6	H9N2	H5N1	H3N8	H10N3	Total*
China	0	1†	26	17	1	2	1	48
Cambodia				1				1
Vietnam	1†							1
Ecuador	1							1
Spain		2†§						2
US		1†§						1
UK		1†§						1
Total*								55

**Case counts may be updated in future reports from the World Health Organization.*
†These cases were initially reported as HPAI A(H5Nx) and later confirmed to be H5N1 virus clade 2.3.4.4b.
§These cases likely represent transient contamination of the nasopharynx/oropharynx after exposure to infected birds.

Spain, the United Kingdom, and the United States, where all detections of H5N1 have occurred in asymptomatic persons with extensive interaction with infected poultry.[353,356,360,361] WHO notification of a laboratory detection in a human with a new subtype of influenza is notifiable under International Health Regulations, and evidence of illness is not required for the report.[357]

In the United States as of March 2023, more than 6,300 people had been monitored following exposure to HPAI A(H5N1) in infected birds or other animals since February 2022.[362]

Additional notes on the first U.S. detection of A(H5N1) virus clade 2.3.4.4b

The first detection of AIV H5N1 in a person in the United States was reported on April 28, 2022. The person resided in Colorado and had extensive contact with sick poultry through participation in the culling process of infected flocks.[258,363] The patient reported only fatigue and was treated with antiviral medication. This is the second detection of A(H5N1) of the clade 2.3.4.4b, with the first case having been reported in the United Kingdom in December 2021.[361] However, two additional similar human detections were reported in September 2022 in Spain. All four detections are being considered cases, with the understanding from WHO that transient contamination cannot be ruled out as the reason for the positive laboratory test.[355] All patients were asymptomatic and were included as part of active surveillance of poultry workers. It is important to note that these detections do not indicate the ability of the HPAI A(H5N1) clade 2.3.4.4b virus to infect humans. The A(H5N1) clade 2.3.4.4b virus is the most common strain circulating among birds internationally.[258] For more information on how this outbreak is affecting birds see Highly Pathogenic Avian Influenza Key Events, International—2020–2023.

This U.S. human detection of A(H5N1) virus clade 2.3.4.4b coincided with a substantial outbreak of HPAI A(H5N1) perpetuating in the domestic poultry population.[364] For more information on this case, the strain, and the current situation visit the following websites:

- 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

Detections of A(H5N1) Virus Clade 2.3.4.4b—2023

Human case detections of HPAI A(H5N1) virus clade 2.3.4.4b have been reported by the WHO since the rise and dominance of A(H5N1) viruses in 2020 (Table 3). Case counts change regularly, as it takes time to confirm influenza subtype, strain, and clade in some human cases. Case counts are

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Table 6 Human infections and detections of avian influenza cases in 2023.[437,438,440]

	A(H5N1) (case)	A(H5N1) (detection)	A(H5N6)	A(H9)	A(H9N2)	A(H3N8)
China	1		4	2	5	1
Cambodia	9			1		
UK		4*				
Chilie	1					
Ecuador	1					

**Based on the available information, WHO considers these as sporadic detections of avian influenza viruses among humans with no evidence of person-to-person transmission to date. More information is available here: https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON468*

routinely updated and aggregated by CDC; see Technical Report: Highly Pathogenic Avian Influenza A(H5N1) Viruses (cdc.gov).[362]

In the U.K., a total of 4 detections of A(H5N1) were reported to the WHO. None of the cases were symptomatic and were detected as a result of extensive monitoring of agricultural workers (Table 6).

One case of A(H5N1) was reported in Chile, another in Ecuador, and 1 in China. All cases had exposure to sick or deceased birds (Table 6).

Human Cases of Avian Influenza (Excluding H5N1 Clade 2.3.2.1b), International—2023

In February 2023, 2 human cases of A(H5N1) clade 2.3.2.1c were reported to WHO by Cambodia. This clade differs from clade 2.3.4.4b, which is actively circulating in the U.S. and other countries. Clade 2.3.2.1c viruses have circulated in Cambodia since 2014.[349] Seven additional cases of Clade 2.3.2.1c were reported through the end of 2023 all with known contact with sick or deceased birds. While not substantiated, person to person transmission could not be ruled out for 2 cases.

Four cases of A(H5N6), 2 cases of A(H9), 5 cases of A(H9N2), and 1 case of A(H3N8) were reported in China (Table 6).

Human Cases of Avian Influenza, International—2024

In 2024, 1 human case of avian influenza A(H5N1) was reported by Vietnam. Another human case was reported by the U.S. in the state of Texas in an agricultural worker whose only symptom was conjunctivitis. The case had exposure to infected cows which were part of an outbreak of HPAI H5N1 clade 2.3.4.4b in cattle in eight states as of April 2024 (Table 7).

Human-to-Human Transmission of AIV and Pandemic Potential

To gain pandemic potential in humans, avian influenza viruses must adapt to easily infect humans, they must spread readily from person to person, and must be a virus to which humans are immunologically naive.[318,325] The HPAI A(H5N1) virus clade 2.3.4.4b virus is continuing to evolve and spread in animal populations, increasing the exposure risk to humans. However, adaptation of the α-2,6 sialic acid receptor, which is required for

Table 7 Human infections and detections of avian influenza cases in 2024.[437,438,439,440]

	A(H5N1) (case)	A(H5N1) (detection)	A(H5N6)	A(H10N5)	A(H9N2)
China				1	3
U.S.	1				
Vietnam	1				

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human infection, has not been detected in widely circulating A(H5N1) viruses. As of early 2023, human infection with H5N1 remains rare and has followed contact with infected, sick, or dead birds.[362,365]

Human-to-human spread has not been detected in cases of A(H5N1) virus clade 2.3.4.4b. Of all AIV human infections reported since 1997, human-to-human spread has only occurred in a small number of people.[343]

The Influenza Risk Assessment Tool (IRAT) is used to assess the pandemic potential of influenza A viruses not currently circulating in people and when compared to other similarly assessed viruses. The HPAI A(H5N1) clade 2.3.4.4b virus was assessed in 2022 and scored at a "moderate" risk level with a potential emergence estimate of 4.4 and a potential impact estimate of 5.1.[110] Additional influenza A viruses of clade 2.3.4.4b were determine to be at similar summary risk levels, but those subtypes were H5N6 and H5N8.[110] For more information, see the Influenza Risk Assessment Tool (IRAT) section.

Avian Influenza Virus (AIV) Surveillance and Epidemiology

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.[26,366] Outbreaks of LPAI and HPAI often result in mass culling of affected flocks and cause significant economic impacts to producers and taxpayers, specifically lost compensation to producers when reimbursed by the government or loss of international trade business due to the hesitancy of other countries to import potentially infected products.[26] 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.

Domestic surveillance and requirements for testing of bird flocks vary by state. All states have a National Poultry Improvement Plan (NPIP) with participating facilities: NPIP Participants States (poultryimprovement.org). NPIP coordinators and testing programs are funded through a cooperative agreement with USDA.[367] Information about state coordinators for testing is available in this online document: OfficialStateAgencies.pdf.

Many states have extensive and sophisticated avian influenza surveillance systems involving poultry producers, processing plants, state animal health officials, and sometimes poultry subject matter experts located at local universities. In some states, every poultry flock is tested serologically just before marketing. If found positive for AI, marketing is postponed until the virus is determined to be no longer circulating among the birds, as shown by polymerase chain reaction (PCR) testing of birds and the environment. NPIP state coordinators solicit avian serum collection for each flock at least annually, though frequency of testing depends on the growing/production period of a flock and the capacity of the producer. Testing typically includes serology to find evidence of recent or past infection and PCR to determine 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.[367]

Requirements for interstate movement of birds or eggs are determined by 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.[367]

USDA APHIS routinely posts U.S. HPAI outbreak information on this webpage: Highly Pathogenic Avian Influenza (HPAI).

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Surveillance of AIV in Wild Birds

US routine surveillance of AIV

The US National Surveillance Plan for Highly Pathogenic Avian Influenza in Wild Birds was implemented in 2015 to maximize the U.S. 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 introduction 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 U.S. Department of the Interior's USGS and Fish and Wildlife Service (FWS), as well as state departments of natural resources.[15,368,369]

Surveillance of AIV in wild birds is specifically targeted toward the following:

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

The following document from USDA APHIS details sampling approaches and responses to wild bird AIV events: Early Detection and Monitoring for Avian Influenzas of Significance in Wild Birds

Another document from the USDA outlines the national approach to AIV surveillance in wild birds: Surveillance Plan for Highly Pathogenic Avian Influenza in Waterfowl in the United States.

The USGS and FWS support surveillance efforts for HPAI in wild birds, as seen in Avian Influenza Surveillance.

Multiple US government and international agencies publish surveillance reports for AIV in domestic and wild (terrestrial and aquatic) birds. Table 8 provides links to these reports.

A list of all State Animal Health officials in the United States and its territories can be downloaded from the following site: Federal and State Animal Health (usaha.org).

National Animal Health Laboratory Network (NAHLN) laboratories are listed online in the following document: NAHLN Laboratories Approved for IAV-A Preparedness and Surge Capacity Testing. 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.[368]

A multidecade review of AIV frequencies 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, and then increased in spring. Higher prevalence was found among females and juvenile birds.[370,371] Longitudinal surveillance infers trends of increasing hemagglutinin (HA) subtype diversity and decreasing AIV prevalence throughout a migration season.[370]

International Surveillance of AIV

All highly pathogenic avian influenza (HPAI) infections of any subtype are reportable to the World Organisation for Animal Health (WOAH), the animal health equivalent to the World Health Organization and the agency that maintains the World Animal Health Information System (WAHIS), which is responsible for tracking such infections.[3,135] Low pathogenic avian influenza (LPAI) infections are only reportable to WOAH by countries that do not have endemic levels of A(H5) or A(H7) activity.[135] Recent reports of outbreaks of reportable animal diseases are published on the

Table 8 Domestic and wild bird avian influenza virus surveillance information and reports—US and international

	United States	International
Avian (domestic)	WHISPers (usgs.gov) USDA APHIS	WOAH-WAHIS
Avian (wild—terrestrial and aquatic)	WHISPers (usgs.gov) US Geological Survey Avian influenza in wild birds	

WAHIS dashboard: WOAH-WAHIS. This interactive dashboard allows search filters for multiple categories.

Another source of detailed HPAI virus detection is the Food and Agriculture Organization (FAO) of the United Nations' EMPRES-I webpage.[372]

Additional collaborative surveillance efforts among wild birds occur through the US Geological Survey (USGS) National Wildlife Center, the National Institutes of Health Centers of Excellence for Influenza Research and Surveillance, the University of Iceland, and others.[132]

Additional AIV Resources can be found at the Avian Flu—FAO's Animal Production and Health Division.

Highly Pathogenic Avian Influenza Key Events, International—2020–2023

Background Lineage and Clade Derivation

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.[11,16] There are additional supporting lineages named for viruses found in Australia and South America.[139,140] North American lineage viruses have not yet been reported in humans.

As mentioned earlier, subtyping of AIVs continues after lineages; viruses can be differentiated by clades and then further differentiated by subclades, also referred to as groups and subgroups, respectively (Figure 2). The clade designation is based on hemagglutinin, not neuraminidase. Clades are organized by similarities in their HA gene sequences, though phylogenic trees may be created for any influenza gene.[11]

Sporadic outbreaks of Eurasian and Asian lineage A(H5) viruses among wild and domestic birds continued in Asia and Europe from 2010–2013.[154-156] In 2010, a genetically distinct clade 2.3.4.4 Gs/GD A(H5N1) lineage HPAI virus emerged, resulting in increasing occurrences of HPAI in wild birds (FIgure 6).[157] The clade 2.3.4.4 virus became better adapted to waterfowl and was then able to cause asymptomatic infections in wild birds.[158]

Origins of the 2020–2023 HPAI A(H5N1) Virus Clade 2.3.4.4b Outbreak

In January 2020, a novel H5N8 virus of the subclade 2.3.4.4b was identified in Poland subsequently causing a widespread outbreak in Europe, Africa, and Asia.[372,373] The strain detected in Poland was believed to have originated in Central Asia.[374] The H5N8 virus reassorted with other influenza viruses, resulting in outbreaks caused by H5N3, H5N4, and H5N5 mainly in Europe, and H5N6 in China where human infections occurred as well.[372,373] For more information on the five human cases of HPAI H5N6 from 2020, see Surveillance for Novel Influenza A Viruses in Humans.

In October 2020, a new reassortant HPAI H5N1virus was detected in the Netherlands that belonged to the 2.3.4.4b clade.[5] The virus retained HA and MP gene segments similar to the H5N8 virus but had reassorted with 4 other viruses (Figure 19).[209] While the H5N8 virus in wild waterfowl initiated the global outbreak, resulting in sporadic outbreaks in domestic poultry, the H5N1 virus soon became the predominant subtype of sustained and even more widespread dissemination of the virus after late 2021.[3,258] Many countries detected epizootic outbreaks among wild waterfowl, many species of which were not overtly affected. Other countries, primarily in Europe and later in North America, experienced outbreaks in domestic poultry. The HPAI H5N1 virus reassortant has now caused the largest international epidemic in birds since 1920, resulting in over 10,000 outbreaks in more than 42 countries and infections detected on every continent except Antarctica.[372,374] In Europe alone, more than 5,000 outbreaks in domestic poultry have been reported, leading to the culling of more than 50 million birds (Figure 20).[373]

Virus detection in far-reaching wild waterfowl breeding locations in the North Atlantic and

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distribution to multiple migratory flyways raise the concern of continued dissemination and possible endemicity in domestic poultry in some countries. Detections of the HPAI virus persist in wild bird populations in Europe. Also of concern, at least eight mammalian species have been infected with the HPAI virus in the European Union.[375]

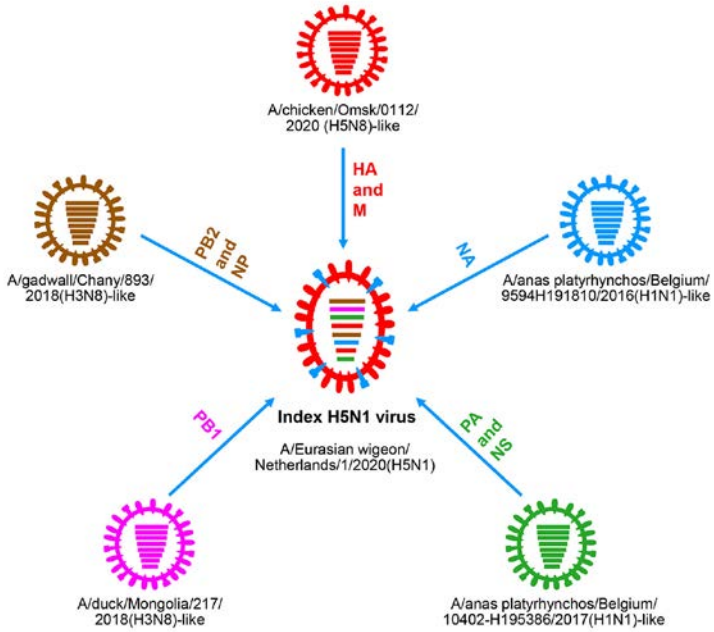
Across the globe, HPAI A(H5N1) virus clade 2.3.4.4b and, to a lesser extent, other avian flu viruses have perpetuated the "largest and most extended epidemic of avian influenza with unusual persistence of the virus in wild bird populations," according to the WHO.[365]

For a detailed chronology of avian flu activity from 2000 forward, go to Highlights in the History of Avian Influenza (Bird Flu) Timeline – 2020-2023 | Avian Influenza (Flu) (cdc.gov).

HPAI A(H5N1) Virus Clade 2.3.4.4b Incursions into Canada and the United States

In October 2021, HPAI A(H5N1) virus clade 2.3.4.4b was detected in 2 different clusters in a resident bird species (white-tailed eagle) and chickens. Migratory birds (geese, gulls, and waders) from the British Isles whose infections with HPAI A(H5N1) virus were confirmed in the summer of 2021 are believed to have spread the virus to resident birds of Iceland before moving to Canada and the eastern coast of the United States (Figure 21).[9] The likelihood of this transmission pathway was reinforced by the detection of the HPAI H5N1 virus in Newfoundland and

Figure 19 Composition of the H5N1 virus containing the 2.3.4.4b HA gene. Source: Shi, et al, 2022.[5]



Labrador, Canada, in December 2021.[9,376,377] This was the first report of HPAI H5N1 virus in the Americas since June 2015, when the virus spread as a result of wild birds migrating across the Bering Strait into Canada and the northeastern United States.[378] There are typically 2 major migrations of wild waterfowl per year, 1 in spring–summer (north to south) and 1 in fall–winter (south to north).[379]

Wild bird samples are routinely collected throughout the United States by the Department of Agriculture, Animal and Plant Health Inspection Service, Wildlife Services, and the National Wildlife Disease Program in the Atlantic and Pacific migratory flyways. Live birds and hunter-killed birds are included in surveillance efforts, which are coordinated by state wildlife agencies and universities. In January 2022, HPAI H5N1 virus clade 2.3.4.4b was detected in 2 wild birds in South Carolina in January 2022. Another avian infection was immediately identified in North Carolina. The birds were outwardly healthy and either trapped live or obtained by hunters. In the 2 months following the initial detections in the Carolinas, 291 additional infections were confirmed in wild birds. North American lineage AIVs were not found in any samples.[377]

In February 2022, the USDA confirmed the first HPAI outbreak in a commercial poultry facility in Indiana followed by outbreaks in Kentucky and Virginia. According to CDC[235], genetic sequence data confirmed viruses from infected poultry aligned with 2.3.4.4b strains found in wild birds.[235] Within the first 2 months of the initial detection of H5N1, domestic poultry outbreaks were confirmed in several states within the Atlantic and Mississippi flyways, indicating infected wild migratory birds had already disbursed widely throughout the U.S. Infections primarily in backyard

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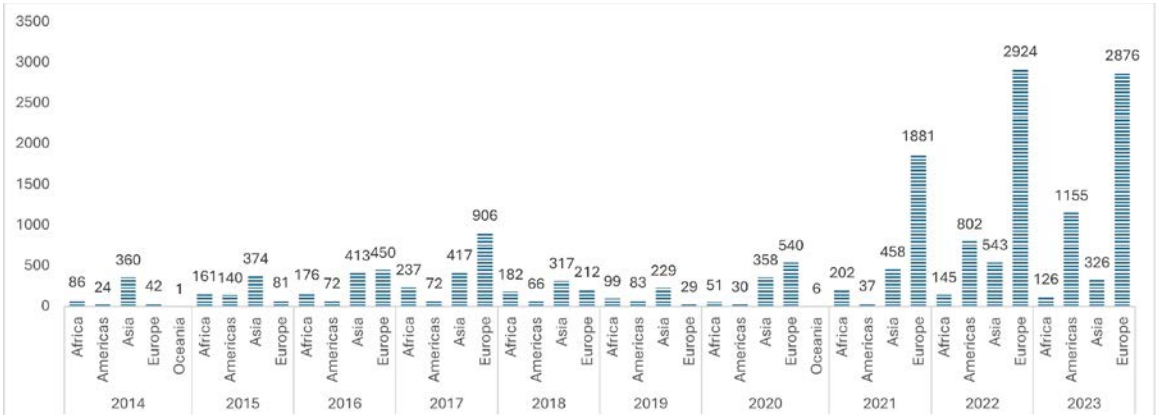
Figure 20 Count of new avian influenza virus outbreaks in birds by month and year.
Source: Adapted from WOAH-WAHIS, 2024.[3]



poultry flocks and several commercial flocks were confirmed in the remaining two flyways, central and pacific, in March 2022.[380]

Detections continued in commercial and backyard flocks with a tremendous number of outbreaks and domestic birds culled throughout the summer of 2022.[3,381,382]

The most recent U.S. HPAI virus outbreak differs from the previous large-scale event from 2014–2015 in multiple ways. This H5N1 2.3.4.4b Eurasian virus strain causes rapid illness and death in poultry. While this virus can infect some waterfowl species without symptoms of illness, it has caused significant mortality in other wild bird species.[380] The highest mortality rates among domestic species is in turkeys, followed by broiler chickens and layer chickens.[383]

The 2014–2015 outbreak was introduced by migratory wild birds but was largely perpetuated by lateral spread from farm to farm.[380] In contrast, during the 2022 outbreak, independent introductions of wild bird-origin H5N1 are believed to have been the cause of disease in approximately 85% of affected commercial and backyard poultry premises.[380]

Also differing from the 2014–2015 outbreak are the types of farms affected. In the earlier outbreak, only 21 backyard flocks were affected, whereas in the most recent outbreak there were more than 450.[380] The increase in affected backyard flocks is attributed to a high amount of virus circulating among wild waterfowl as well as an increase in the number of backyard flocks experienced during the COVID-19 pandemic.[384]

Throughout the 2022–2023 event, Minnesota had the largest number of flocks with outbreaks, while Iowa had the most significant poultry loss, with 16 million birds culled at the time of publication, followed by Nebraska, Colorado, and Pennsylvania.[382] To view the most recent case counts, go to: HPAI Confirmations in Commercial and Backyard Flocks (usda.gov). By March 2023, almost 60 million birds were affected in more than 300 commercial flocks and over 450 backyard flocks were affected in all states except Hawaii, Louisiana, and West Virginia.[382]

Impact on Mammals—International and United States

Unlike previous HPAI virus outbreaks, H5N8 in 2020 and H5N1 shortly thereafter infected many species of mammals in multiple countries. Some recent infections have caused severe illness with neurologic symptoms.[365] In 2020, H5N8 was detected in seals and a fox.[216] In 2021, H5N8 infections in seals were reported in the United Kingdom, Germany, and Denmark.[192] Given seals mainly consume fish, it is believed seals are acquiring infection from environmental contamination. Seals are often located around migratory birds who contaminate the ground and sea with feces.[318] In May 2021, an outbreak of H5N1 among wild fox kits was reported in the

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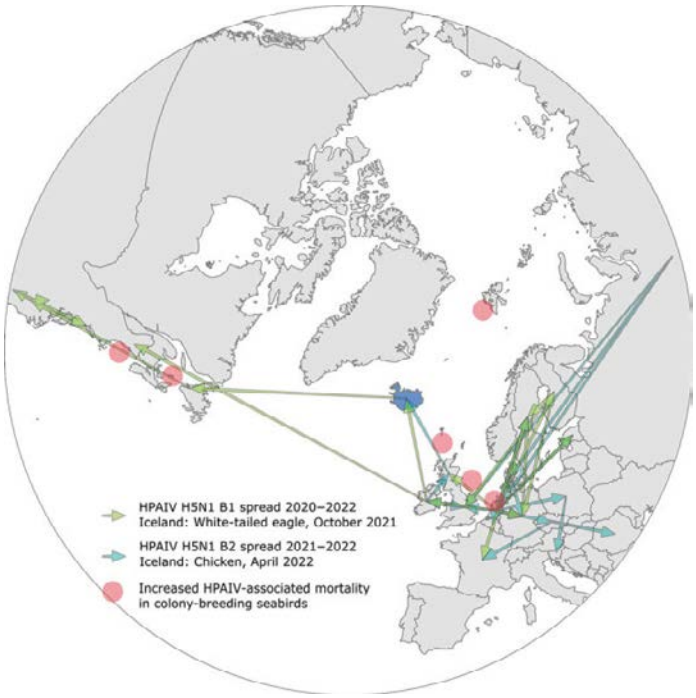
Figure 21 Polar map view of the palearctic and near arctic realm, and inferred spread of hemagglutinin clusters B1 and B2 of highly pathogenic avian influenza viruses (HPAIVs), subtype, clade 2.3.4.4b and their incursion routes to Iceland (blue) during 2022. Source: Gunther, 2022.[9]



Netherlands at the same time as an outbreak among wild birds.[386] Other detections have included polecats, otters, and badgers.[387]

In early 2022, an outbreak of H5N1 that started in pelicans in Peru spread to sea lions, resulting in more than 3,000 deaths of these animals.[230,388] In October 2022, an outbreak of HPAI A(H5N1) clade 2.3.4.4b in minks was reported in Spain. While mink-to-mink transmission was suspected, these minks were continuously exposed to wild birds throughout the outbreak which cannot be ruled out as the sole source of infection.[389] Mammalian infections were also identified in zoo animals, such as tigers and leopards, after the animals had been fed infected bird carcasses.[390,391]

Since HPAI A(H5N1) virus clade 2.3.4.4b was detected in the United States in 2022, at least 15 species of mammals have been infected with the virus. The most commonly affected species are the red fox, followed by the harbor seal, mountain lion, raccoon, striped skunk, and bobcat.[392] To view the most recent case counts in mammals, go to: HPAI Detections in Mammals (usda.gov). Mammalian infections have been reported primarily in northern and north-central states, with overlap between wild bird detections and commercial poultry outbreaks.[392] Some genetic sequences of viruses involved in these infections exhibited evidence of mammalian adaptation, particularly at the PB2 gene.[386,387] However, several other avian influenza viruses have adapted to mammals in the past, and these adaptations do not indicate the ability for mammal-to-mammal spread of the virus. Also, significant additional adaptation would be required for this HPAI A(H5N1) virus to infect humans.[318]

Globally, infections with H5N1 subclade 2.3.4.4b viruses have been detected in the following mammals: badger, black bear, bobcat, coyote, dolphin, ferret, fisher, cat, fox, lynx, mink, opossum, otter, pig, polecat, porpoise, raccoon, raccoon dogs, seal, and skunk.[365] Additional infections among scavenger species are expected with counts updated by the USDA APHIS.[392]

Avian Influenza Virus General Prevention and Control Guidelines

Transmission Among Birds and Between Birds and People

AIV is most commonly spread from birds to other susceptible hosts through the feces or secretions from the nose, mouth, and eyes of infected birds (Figure 22). 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 22).[237,393,394]

AIV Transmission From Food

In general, human infection with an AIV is an occupational hazard and not evidenced as a food safety concern.[394] Eggshells can contain AIV on their surface

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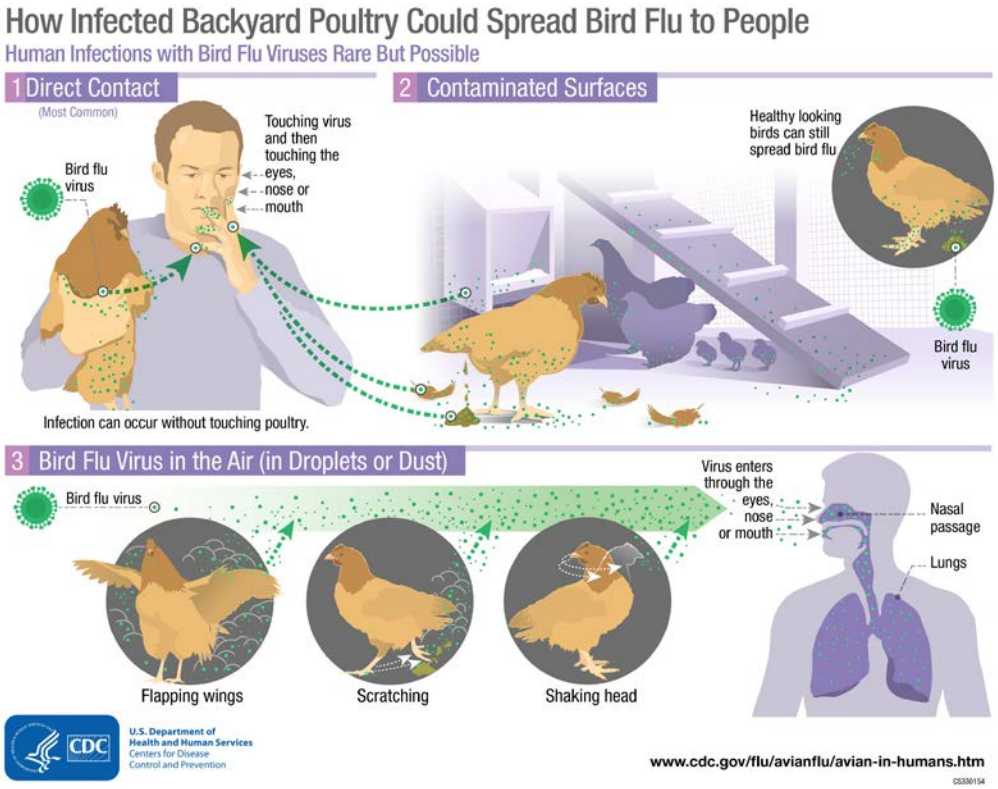
Figure 22 How infected backyard poultry could spread bird flu to people. Source: CDC, 2023.[393]



and are therefore a potential vehicle for transmission. Proper handling and cooking of eggs will kill AIV.[394] 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.[148,393] In at least one 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.[395]

Production Controls and Interstate Transport

In the United States, the National Poultry Improvement Plan (NPIP), in cooperation with USDA and state animal health officials, provides the framework to manage poultry flock testing and certification required for interstate transport. Certification status by state is listed on the NPIP site: NPIP Participants States (poultryimprovement.org). State NPIP coordinators regularly offer biosecurity training for producers from commercial entities (sectors 1 or 2) to backyard flock owners.[367]

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 state-level plans. 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 does include AIV guidance.

International Prevention and Control Efforts

The World Organisation for Animal Health (WOAH; formerly known as the Office International des Epizooties [OIE]) was formed in 1924 through an international agreement.[102] The WOAH is responsible for improving animal health and publishes animal-specific terrestrial reference guides. The WOAH is recognized by the World Trade Organization and includes a total of 182 member countries with regional and subregional offices on every continent.[102]

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WOAH maintains a list of 204 notifiable terrestrial and aquatic animal diseases. Highly pathogenic avian influenza and equine influenza virus infections are included.[3,135,396,397] Countries with endemic LPAI A(H5) or A(H7)activity may choose to report their status to WOAH as well. The entire list is located here: Animal Diseases - WOAH - World Organisation for Animal Health. As previously stated, the WOAH closely tracks AIV outbreaks on a publicly available dashboard and produces routine reports.[3]

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 WOAH, United Nations Food and Agriculture Organization (FAO) their joint organization, which is referred to as OFFLU, the World Health Organization (WHO) and the United Nations Environment Programme (WOAH, UNEP, FAO, and WHO are the quadripartite partners). Their response plans and cross-collaboration documents are located as follows:

- Global consultation on highly pathogenic avian influenza (HPAI) (fao.org)
- Global AIV with Zoonotic Potential (fao.org)

WOAH 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. …"[398] Click on this link for the chapter: Terrestrial Code Online Access — Chapter 10.4. The WOAH *Terrestrial Manual* includes a chapter on avian influenza (including infection with highly pathogenic avian influenza viruses) that provides an extensive overview of the pathogen and its manifestations in birds, the potential of the pathogen to spread beyond its host species, and prevention and control of infections and outbreaks. That chapter can be accessed at Terrestrial Manual — Chapter 3.3.4.

Quadripartite+: One Health Initiative (who.int)

OFFLU: OFFLU Network on Avian Influenza

WHO: Influenza (avian and other zoonotic)

Quadripartite Guide to addressing zoonotic diseases in countries: One Health Joint Plan of Action Launched and Presented by WHO and the Quadripartite Partners

International commodities resources

- Canada - Avian Commodities
- Canada - Hunter Harvested Wild Game Bird Carcasses
- Japan – Avian Commodities
- Mexico - Avian Commodities
- Norway - Avian Commodities
- Switzerland, Canton of Zürich - Avian Commodities
- Switzerland, Canton of Jura - Avian Commodities

HPAI Outbreak Prevention Guidance—United States

Domestic Poultry and Backyard Flocks

Lessons learned from the 2014–2015 U.S. HPAI outbreak have resulted in substantial improvements in preventing the lateral (i.e., farm-to-farm) spread of avian influenza. According to APHIS, approximately 85% of U.S. outbreaks are genetically related to wild bird-origin H5N1 strains.[380]

There are many known risk factors for the spread of HPAI between domestic poultry flocks (Figure 23) including[380,399]

- Movement of live and dead birds
- Transportation of manure
- Employee movement between farms and with employees of other farms
- Equipment sharing across multiple farms
- Contaminated feed trucks, vehicles, water, and people
- Visitors to the farm and employee connections with other farms

Additional drivers of HPAI in domestic poultry outside lateral transmission typically involve interaction between wild birds and domestic flocks. This may occur when water sources for domestic poultry are shared with infected wild birds.[400] Feces from infected wild birds may be tracked into barns by workers. There is also the possibility of direct interaction between wild birds and domestic poultry if barns are kept open to promote "free range" accessibility for domestic birds.[380]

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Passive Surveillance and Key Biosecurity Measures—Domestic and Backyard Flocks

Multiple overlapping approaches to passive surveillance of domestic and backyard flocks are recommended.

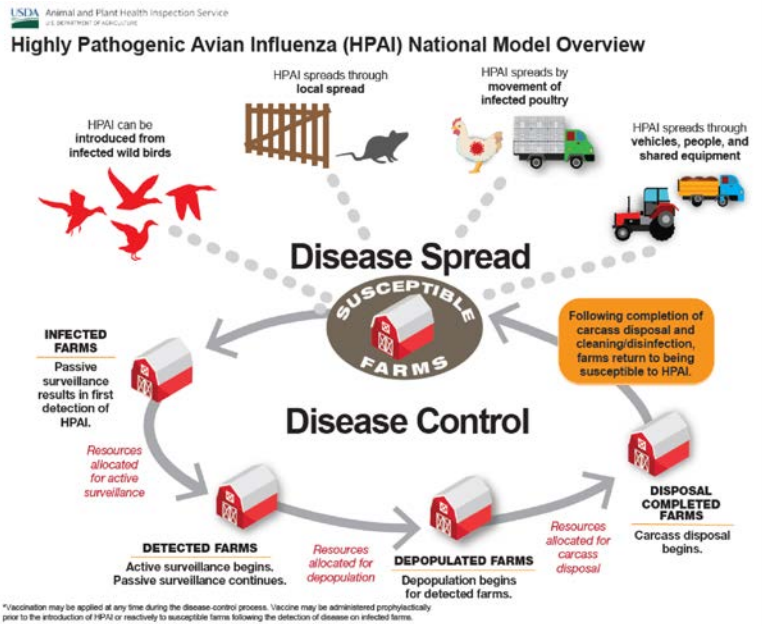
Surveillance for illness in birds[401]

- Guidance
  - Sudden death without clinical signs
  - Lack of energy and appetite
  - Decreased egg production or soft-shelled or misshapen eggs
  - Selling of head, comb, eyelid, wattles, and hocks
  - Purple discoloration of wattles, comb, or legs
  - Nasal discharge, coughing, and sneezing
  - Lack of coordination
  - Diarrhea
- Resources
  - USDA APHIS | Avian Influenza
  - USDA APHIS | Defend the Flock - Signs of Illness

Biosecurity measures[402]

- Guidance
  - Keep visitors to a minimum
  - Wash hands before and after encountering live poultry
  - Provide disposable boot covers and/or disinfectant footbaths for anyone having contact with your flock
  - Change clothes before entering poultry areas before exiting the property
  - Clean and disinfect tools or equipment before moving them to a new poultry facility
- Resources

Figure 23 Highly pathogenic avian influenza national model overview



  - Manage Wildlife To Prevent Avian Influenza
  - Prevent Avian Influenza at Your Farm: Improve Your Biosecurity with Simple Wildlife Practices
  - Improving Biosecurity with Wildlife Management Practices: Reducing Water Access
  - Improving Biosecurity with Wildlife Management Practices: Protecting Food Resources
  - USDA APHIS | Defend the Flock - Biosecurity 101

Recommendations for long-term mitigation[375]

- Guidance
  - Regular maintenance and repair of buildings
  - Systematic implementation of reliable cleansing and disinfection of any equipment
  - Storage of materials in areas protected from direct or indirect contact with wild birds
  - Early testing and rapid reporting of outbreaks in flocks[375]
  - Monitoring aggregation and proximity of wild, migratory birds during periods of an outbreak on local or regional farms
- Resources
  - Improving Biosecurity with Wildlife Management Practices: Preventing Access to Barns and Other Facilities
  - BirdCast – Live Bird Migration Maps

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Prevention Against Avian Influenza Infection and Illness in Humans

Human exposure to HPAI A(H5N1) is highest among poultry workers, backyard flock owners, veterinarians, and animal health officials, including those involved in de-population following HPAI outbreaks. Recommended personal protective equipment (PPE) includes:[403]

> *Properly-fitted unvented or indirectly vented safety goggles, disposable gloves, boots or boot covers, a NIOSH-approved respirator (e.g., N95), and disposable fluid-resistant coveralls, and disposable head cover or hair cover.*

Additional protections include the following[375]:

- Foot baths for cleaning and disinfecting shoes before entering barns
- Training workers on the appropriate use of PPE
- Physical distancing, enhanced ventilation, dust, and aerosol-avoiding measures
- Separation of street clothing and work PPE

The seasonal influenza vaccine is recommended for potential responders to avian influenza situations involving birds as well as for poultry workers. This reduces the risk of co-infection with a seasonal strain and avian strain.

Additional details on worker protections are located at the following sites:

- Recommendations for Worker Protection and Use of Personal Protective Equipment (PPE) to reduce exposure to novel influenza A viruses associated with severe disease in humans.
- NIOSH Alert: Protecting Poultry Workers from Avian Influenza (Bird Flu) (document includes instructions in Spanish)
- eTool: Respiratory Protection | Occupational Safety and Health Administration (osha.gov), including guidance on how to fit test poultry workers for N95 respirators.

Additional Disease Prevention Resources—Domestic Flocks

Numerous resources are available on the USDA APHIS Flock Defender website: USDA APHIS | Defend the Flock - Resource Center. Topics covered include biosecurity basics and videos, webinars, the Defend the Flock toolkit, wildlife management, partner materials, and USDA and other federal agency resources.

Additional Disease Prevention Resources—Backyard Flock Owners

- Backyard Flock Owners: Take Steps to Protect Yourself from Avian Influenza
- Prevention and Antiviral Treatment of Bird Flu Viruses in People
- USDA APHIS | Defend the Flock - Resource Center

The USDA has compiled guidance on cleaning and disinfecting premises contaminated with HPAI:

- Avian Influenza Basics for Urban and Backyard Poultry Owners| UMN Extension
- Cleaning & Disinfection Basics (Virus Elimination)
- Checklist for Cleaning and Disinfecting Poultry Enclosures
- Checklist for Managing Poultry Manure and Litter
- List M: Registered Antimicrobial Products with Label Claims for Avian Influenza

Disease Prevention Resources—Wild Birds, Wildlife Refuge, and Hunters

- Hunters - Protect Yourself and Your Birds From Avian Influenza
- Protecting Captive Wild Birds From Highly Pathogenic Avian Influenza
- Guidance for Zoos and Captive Wildlife Facilities: Protecting Birds From Highly Pathogenic Avian Influenza
- Hunter Wallet Card

Posters and Signs for Use in Agricultural Fairs, Markets, and Trade Shows

- Poultry Owners: Report Sick Birds!
- Stop Avian Influenza Outbreaks

HPAI Outbreak Control Guidance—United States

Commercial or Backyard Flocks

The USDA or state officials are responsible for managing the response to an HPAI outbreak. According to the USDA,[100]

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If your birds appear sick, USDA or State officials will collect samples from your flock to check for HPAI. We may also test your flock without you reporting sick birds if HPAI has been detected elsewhere in your local area. We will send the samples to a nearby laboratory in the National Animal Health Laboratory Network for preliminary testing. This network includes State, university, and Federal laboratories throughout the United States that have the capacity to handle a large volume of testing and give results quickly—in most cases, the same day a lab receives samples. We will also send samples to the National Veterinary Services Laboratories (NVSL) for confirmation. NVSL is the official reference laboratory for foreign animal disease testing, including HPAI, in the United States. NVSL usually takes 1–2 days to complete this work, but it can take longer, and we may need to collect additional samples to complete the testing.

Contact information for USDA as well as for state animal health officials is listed in Appendix A. State agencies have differing roles in helping manage HPAI outbreaks depending on the state.[325,399,404-406] State public health veterinarians and/or state veterinarians may provide outbreak response resources to producers or owners of backyard flocks.

The Highly Pathogenic Avian Influenza Response Plan: The Red Book is a comprehensive document produced by USDA APHIS for the remediation of HPAI situations. A reference document on the Red Book is located here. Links to subsections of the guide plus resources from the Foreign Animal Disease Preparedness and Response Plan (FAD PReP) are listed below with their revision dates.[368] These documents are intended for use by commercial producers or backyard flock owners preparing to experience or experiencing an outbreak of HPAI. While these documents were primarily updated or produced in response to HPAI A(H5N1) clade 2.3.4.4b, they are relevant for emergency response and control of outbreaks of HPAI of any strain. Document links are provided in lieu of document content as the content is likely to change over time.

The following resources are specific to outbreaks on commercial or backyard flock premises. Where applicable, section headers indicate whether documentation is relevant for flock owners or state animal health officials.

Initial response

Commercial and backyard flock owners

- Highly Pathogenic Avian Influenza: What To Expect at the Start of an Outbreak
- VS Guidance 12001.4 Ready Reference Guide: Procedures and Policy for the Investigation of Potential Foreign Animal Disease (FAD)/ Emerging Disease Incidents (EDI) 7/23
- USDA Authorization for Response and Associated Activities 4/22
- Response Goals & Depopulation Policy 1/22
- Ventilation Shutdown Plus (+) Policy 1/22
- Permitting Live Poultry into an Infected Zone: Claims for USDA Indemnity Not Considered 4/22

State public health/animal health officials

- HPAI New State Checklist 2/23
- Initial Epidemiological (Epi) Interview 11/22
- EMRS 2.0: Quick Reference for HPAI Disease Management 5/22

Finance and administration

Compensation information for owners

- Highly Pathogenic Avian Influenza: Indemnity and Compensation When Your Flock Is Infected
- Overview of Finance and Administration Procedures 2/22
- Emergency Cooperative Agreement Guidance: Financing the Response: State/Tribal Information 1/23
- Poultry Indemnity Valuation for HPAI 1/23
- VSG 8603.2 - Procedures for Indemnity and Compensation Claims in Cases of H5/H7 LPAI in Poultry 5/21

Appraisal and indemnity request forms

- □ Appendix 1H – Indemnity and Compensation Request for HPAI 5/23
- □ Appendix 2H - HPAI-Affected Backyard Flock Management Agreement 1/23
- □ Appendix 2A – Draft for Poultry Owner 2/22
- □ Appendix 2B – Draft for Contract Grower 2/22
- □ Commercial Flock Plan: H5/H7 AI Euthanasia/ Depopulation, Disposal, & Virus Elimination Procedures for Commercial Infected Premises 4/22

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- Backyard Flock Plan: H5/H7 AI Euthanasia/ Depopulation, Disposal, & Virus Elimination Procedures for Backyard Infected Premises 4/22
- HPAI Virus Elimination: Per-Cubic-Yard Flat Rates for Table Egg-Laying Bird Barns and Table Egg Storage and Processing Facilities 5/23
- HPAI Virus Elimination: Per-Square-Foot Flat Rates for Floor-Raised Poultry

Surveillance and diagnostics

- Avian Sample Collection for Influenza A and Newcastle Disease 1/23
- Surveillance of Backyard Flocks Around Infected Premises 5/22
- Surveillance Sampling for Commercial Premises in Control Area 5/22

Quarantine, movement control, and continuity of business

Commercial and backyard flock owners

- HPAI Zones and Premises 5/17
  - Training PowerPoint 4/16
- Movement Control 6/22
- Testing Requirements for Movement from the Control Area 6/22

State public health/animal health officials

- Overview of the HPAI Control Area Permitting Process 2/22

Disposal & cleaning/disinfection

Commercial and backyard flock owners

- Mortality Composting Protocol for AI Infected Flocks 2/16
- Job Aid: Overview of the HPAI Composting Process 5/16
- Mortality Composting: Pre-Compost Windrows for Avian Influenza Infected Flocks 5/16
- Mortality Composting: Carbon Sources for Windrow Construction 5/16
- Finding Carbon Source: What to Say When Calling Potential Vendors 12/16
- Mortality Composting: Windrow Construction Protocol for Avian Influenza Infected Flocks 5/16
- Mortality Composting: Temperature Monitoring Protocol of Avian Influenza Infected Flocks 5/16
- Calibration of Analog Thermometers 3/16
- Mortality Composting: Compost Windrow Construction Approval Checklist for Avian Influenza Infected Flocks 5/16
- Mortality Composting: Phase 1 Windrow Evaluation Checklist Days 1–14 for Avian Influenza Infected Flocks 5/16
- Mortality Composting: Phase 2 Windrow Evaluation Checklist Days 14–28 for Avian Influenza Infected Flocks 5/16
- Cleaning & Disinfection Basics: Virus Elimination 10/22
- Using Heat Treatment for Virus Elimination 4/22
- EPA List M: Registered Antimicrobial Products with Label Claims for Avian Influenza
- Setting Up and Operating a Cleaning and Disinfection Station (scroll down on webpage for proper section)

State public health/animal health officials

- Landfill Disposal Guidance—Recommended Waste Acceptance Practices for Landfills 1/23
- CDC Interim Guidance for Landfill Workers
- Landfills and HPAI Response Presentation

Recovery and restocking

- Highly Pathogenic Avian Influenza: Restocking Your Poultry Flock
- Control Area Release 5/22
- Timeline, Eligibility, and Approval for Restocking 2/22
- Example Restocking Form 5/22
- Post C&D Environmental Sampling Guidance - Poultry (usda.gov)

FAD PReP – standard operating procedures

- Overview of Etiology and Ecology
- Communications
- Health and Safety & PPE
- Biosecurity

HPAI Ready Reference Guides

- HPAI 2016 Outbreak
- Etiology and Ecology
- HPAI Zones And Premises
- HPAI Diagnostics
- Common Operating Picture
- Quarantine, Movement Control, and Continuity of Business
- EMRS2 Customer Permit Gateway
- Additional Guidance

Live Bird Marketing System Resources

There are approximately 87 live bird markets in the United States, primarily in New York, New Jersey, and Pennsylvania. Markets exist to a lesser extent in Rhode Island, Massachusetts, Connecticut, Maine, and California. The concentration of live bird markets in the northeastern United States

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is attributed to the influx of immigrants from Asia, Africa, and the Middle East.[407]

Outbreaks of HPAI A(H5N1) virus clade 2.3.4.4b have occurred in live bird markets in the United States but were rapidly mitigated. Extensive testing prior to bird movement, onsite market testing, and thorough disinfection procedures have mitigated the impact of the HPAI outbreak.[404] There can be significant human health considerations when HPAI is found in live bird markets, with potential exposure of employees and customers, some of whom may be difficult to track.

The USDA provides Uniform Standards for Prevention and Control of H5 and H7 Avian Influenza in the Live Bird Marketing System: Prevention and Control of H5 and H7 Avian Influenza in the Live Bird Marketing System (usda.gov)[237]

Additional guidance specific to the HPAI outbreak is provided in the following link: HPAI in the Live Bird Marketing System 2/22

A detailed article on live bird markets and successful efforts to mitigate H5/H7 outbreaks is Live Bird Markets of the Northeastern United States - PubMed (nih.gov)[407]

Backyard Flock Resources

The most recent U.S. outbreak of HPAI has significantly affected backyard flocks, therefore, flock owners must practice good biosecurity methods when interacting with sick birds and in preventing contact between domestic and wild birds.

CDC provides the following recommendations for flock owners who must handle sick domestic birds[408]:

- *Use protective equipment like gloves, an N95 respirator if available or, if not available, a well-fitting facemask (e.g., a surgical mask), and eye protection.*
- *Wash your hands with soap and water after touching birds.*
- *Use coveralls, boot covers, and footbaths to reduce transmission between barns and to protect poultry workers.*
- *Avoid touching your mouth, nose, or eyes after contact with birds or surfaces that may be contaminated with saliva, mucous, or feces from wild or domestic birds.*
- *Change your clothes before contact with healthy domestic poultry and handling wild birds, captive wild birds, farmed birds, and other pet birds. Then, throw away the gloves and facemask, and wash your hands with soap and water.*
- *CDC has more information available on what to do after you have been exposed to infected poultry or other birds.*

Specific recommendations for backyard flock owners to take steps to protect themselves from avian influenza (bird flu) are located on the CDC webpage entitled Backyard Flock Owners.

The following are additional recommendations for backyard flock owners:

- Cleaning & Disinfection Basics (Virus Elimination) 5/22
- Checklist for Cleaning and Disinfecting Poultry Enclosures 11/18
- Checklist for Managing Poultry Manure and Litter 2/20
- How to Keep Your Backyard Flock Safe from Bird Flu 1/23
- Avian Influenza Basics for Urban and Backyard Poultry Owners | UMN Extension

Wildlife, Zoos, Rehabilitation Centers, and Hunters

Suspected cases or outbreaks of HPAI in zoos, animal rehabilitation centers, or other domestic environments should also be reported to APHIS. Response guidance may not include immediate culling of the animal, as other protocols may be used for single cases or small numbers of affected animals.[408,409]

The following documents contain guidance for wildlife, zoos, and other captive animal organizations detailing prevention and control measures for HPAI.

- Avian Influenza | US Fish & Wildlife Service (fws.gov)
- Find a Migratory Bird Rehab Facility (arcgis.com)
- What to Do If You Find a Baby Bird, Injured or Orphaned Wildlife
- Letter to Native American Tribal Leaders Regarding Avian Influenza
- Migratory Bird Banding Operations and Considerations During Confirmed HPAI Detections

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- Protecting Captive Wild Birds From Highly Pathogenic Avian Influenza
- Guidance for Zoos and Captive Wildlife Facilities: Protecting Birds From Highly Pathogenic Avian Influenza

Hunters who handle wild birds should be familiar with guidance to prevent the spread of illness. Wild birds should be dressed in the field using good hand hygiene. This should include wearing gloves, an N95 respirator, and using eye protection. PPE should be discarded after use. For more information on hunter safety, review Avian Influenza | U.S. Fish & Wildlife Service (fws.gov).

Public Health Monitoring of Humans Exposed to HPAI A(H5N1)

Following identification of HPAI-infected birds or mammals, state or local public health officials conduct contract tracing to identify and monitor individuals potentially exposed to the virus without wearing appropriate PPE.[325-327] Exposed individuals may include anyone in contact with sick or infected birds, facilities, or farming equipment such as farm workers, persons who routinely visit farm facilities, persons who operate farm equipment, persons who transport animals, persons who process animals, and personnel responding to wild waterfowl die-offs, wild or sick marine animals, or commercial poultry. Any person exposed to HPAI is recommended to be monitored for symptoms of illness for up to 10 days after the exposure. Monitoring includes communication with the exposed individual, asking for the presence of symptoms and coordination for testing if symptoms appear. CDC may request that jurisdictions report monitored individuals to CDC as part of national surveillance efforts.[326,327] CDC should also be notified of testing performed for a person with recent HPAI exposure.[14] Persons who are exposed to HPAI are not generally required to quarantine during their monitoring periods.[14,326]

Guidance for public health surveillance of HPAI-exposed individuals can be found at Public Health Monitoring Plan for USDA/APHIS Responders to Detections of Avian Influenza Virus in Poultry

The suggested CDC definitions for tracking and reporting human infection with avian influenza is located at Case Definitions for Investigations of Human Infection with Avian Influenza A Viruses in the United States (cdc.gov)

Testing guidance for persons with suspected avian influenza is available at Interim Guidance on Testing, Specimen Collection, and Processing for Patients with Suspected Infection with Novel Influenza A Viruses with the Potential to Cause Severe Disease in Humans

The CDC Influenza Division has an emergency contact line that is staffed 24/7. This number may be used by public health officials at any time for questions related to avian influenza human exposures, testing, or illness: CDC Influenza Division: 404-639-3747. Additional contacts include CDC INFO on (website): Contact CDC-INFO; 800-CDC-INFO (800-232-4636); and TTY: 888-232-6348.

Local healthcare providers and other community organizations are encouraged to contact their respective health department regarding infectious disease concerns. 24/7 contact information is available at: https://www.cste.org/page/EpiOnCall.

State Best Practices

The majority of U.S. states now have experience in responding to and mitigating outbreaks of HPAI A(H5N1). Several states began developing best practices after the 2014–2015 outbreak and strengthened or expanded their practices with the 2022 outbreak. The following details a few examples of best practices in U.S. states.

An interdisciplinary committee and centralized testing facilities in Minnesota[325]

In this state, an Emergency Disease Management Committee led by the Board of Animal Health (BAH) serves as a collaborative body for the planning, prevention, response, and control of LPAI and HPAI introductions and outbreaks. The group is comprised of state animal health officials, producers, poultry companies and their veterinarians, USDA APHIS poultry specialists, University of Minnesota poultry experts, university extension agents, and state public health officials. Regular communication regarding situations of interest, in addition to regular meetings led by the Minnesota Board of Animal Health for information exchange, have promoted trust and cooperation across the committee. The HPAI and LPAI outbreak response is a coordinated effort utilizing resources from multiple state and federal agencies along with industry representatives. Information on flocks determined positive for the virus is shared immediately with no barriers to initiating a

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response. For more information, see Avian Influenza | Minnesota Board of Animal Health (mn.gov).

Rapid fit testing training for producers in Iowa[399]

In Iowa, state health officials noticed producers were struggling to rapidly implement fit testing protocols for poultry workers exposed to infected birds. The state worked with the Iowa State University Extension Service to establish training for setting up a fit testing program that includes a respiratory safety clearinghouse. For more information, see Avian Influenza | Iowa Department of Agriculture and Land Stewardship (iowaagriculture.gov). Additional fit testing and OSHA-related information on how to reduce exposure to novel influenza A viruses associated with severe disease in humans can be found at Recommendations for Worker Protection and Use of Personal Protective Equipment (PPE) and at Respiratory Protection - Training Videos | Occupational Safety and Health Administration (osha.gov).

Establishing standards for live bird markets in New York City[404]

One of the few places in the United States with live bird markets is New York City with movement of birds between New York, New Jersey, and Pennsylvania.[404] When the HPAI A(H5N1) outbreak struck the east coast in 2022, the markets were initially closed and then reopened with extensive guidance and protocols provided by animal health officials. State officials had to consider the movement of birds across state lines, which required strict testing protocols before the birds could be moved to ensure new introductions of HPAI did not occur in live markets. The city expanded protocols for cleaning and sanitizing bird housing, equipment, and facilities. These same protocols may be relevant and useful for agricultural fairs outside municipal settings. For more information, see Poultry | Agriculture and Markets (ny.gov).

Swine Influenza Epidemiology, Surveillance, Prevention, and Control

Epidemiology

Swine influenza virus (SIV) is common in swine populations. Internationally, 25% of swine exhibit evidence of serologic immunity to cH1N1; serologic evidence is 30% in U.S. herds and greater than 50% in the North Central United States.[410] SIV circulates seasonally at endemic levels but can also emerge as abrupt epidemics having 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.[411]

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 to potentially find spillover events in which human seasonal influenza has infected pigs.[242]

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) (see the IAV-S Surveillance section).

Influenza Surveillance and Monitoring of Swine Workers

People who work with swine should be familiar with the symptoms of influenza. Seasonal flu viruses can be transmitted from workers to pigs. Workers who experience symptoms of influenza-like illness (ILI) should notify their supervisor and employer, and be referred to a healthcare provider to determine the need for testing and prescription for antiviral medication if appropriate (ideally within 2 days of symptom onset).[324]

Swine workers with ILI should limit contact with other people and limit travel for at least 24 hours after a fever is gone.

Healthcare providers caring for patients who have ILI and have recent swine exposure should contact their local or state health department for additional influenza specimen testing.[324]

Novel Influenza A Surveillance in Humans (CDC FluView): https://gis.cdc.gov/grasp/fluview/Novel_Influenza.html

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Surveillance of Swine

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 (WOAH).[412] 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.[14,411] Since influenza is endemic in swine populations, reporting of SIV is not required per WOAH.[413] The USDA focuses testing efforts on swine populations meeting the following criteria:

- Farms with pigs exhibiting symptoms of influenza-like illness (ILI)
- Swine exhibiting ILI at concentrated gatherings such as auctions, markets, fairs, or exhibition events
- Swine epidemiologically linked to a confirmed case of SIV in a human[411]

The National Surveillance Plan for Swine Influenza Virus in Pigs is published by USDA APHIS and includes testing strategies and protocols for the epidemiologic investigation of SIV in swine.[411]

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, and is the origin of substantial exports.[411] The risks of not increasing the scale and scope of surveillance include the following:

- Potential for emergence of a pandemic influenza virus;
- 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
- 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 restrictions[411]

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. Twelve states reported cases, with the majority of cases split between Indiana and Ohio (Table 9). All individuals reported direct or indirect contact with swine, primarily at agricultural fairs. The median case-patient 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 (PCR) testing, especially when influenza is suspected outside of typical seasonal prevalence periods.[341]

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.[68]

Table 9 Human infections with swine influenza virus, 2011–2012

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

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SIV poses no risk of infection when properly cooked swine meat is consumed by humans.[68]

The FluView novel influenza dashboard only provides data through the last 10 years. The following CDC site contains detailed case reports of novel infections before 2013: Reports of Human Infections with Variant Viruses.

Human infections of SIV following the period 2012–2017—United States

The second largest human outbreak of novel influenza to date in the United States occurred in 2017 and was also attributed to an A(H3N2)v virus. Exposure to swine 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.[414]

Human outbreaks of SIV—United States and International

SIV infections in humans are tracked internationally by the WHO in the same way that AIV infections in humans are tracked: through semi-monthly 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.[14,347] Given the widespread distribution of swine facilities, the 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 of SIV, 19 with A(H1N1)v and 2 with A(H3N2)v, 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 extensive surveillance, testing, and reporting, but also because of the extensive interaction between humans and swine, whether through production, farm exposure, agricultural fairs, etc.[350] Four U.S. states reported cases in 2021–2022—Ohio, Iowa, Wisconsin, and North Carolina—all with robust swine industries.[3] As previously stated in the Human Influenza Surveillance and Epidemiology section, human SIV infections vary greatly by year. A(H3N2)v cases occurred more commonly in previous years, but now A(H1N1)v cases are more prominent in the United States and internationally (Figure 24).[2]

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—WOAH—World Organisation for Animal Health
- VS Contacts: Area Offices and State Animal Health Official Directory
- Testing Guidelines, Forms, and Submission Instructions
- Influenza A in Swine Testing Algorithm Instructions
- Participating NAHLN labs
- Notification Plan for a Novel Influenza A Virus 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

Figure 24 Novel influenza A virus infections in humans in the United States.
Source: CDC FluView 2024.[440]

	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	2022-23	2023-24	Total
Influenza A H1N1v	0	2	2	0	3	1	0	1	1	0	8	0	0	0	18
Influenza A H1N2v	0	4	0	0	0	3	4	14	0	0	4	6	2	1	38
Influenza A H3N2v	7	315	20	3	3	19	61	2	0	1	2	5	1	0	439
Influenza A H7N2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Influenza A H1v	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Influenza A H3v	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Influenza A H5N1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2
Total	7	321	22	3	6	23	66	17	1	1	14	13	4	2	500

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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. [150,397,410,415] SIV spreads easily from infected herds to uninfected herds, by people and equipment shared between infected and uninfected herds, or by the introduction of new stock to an infected herd.[411]

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, sometimes for extended periods. Fecal contamination in a watering pond or other water sources, whether used for swine consumption or cleaning, can result in exposure. Multiple reassortant strains have resulted from swine exposure to AIV.[30,411,416,417]

Conversely, SIV from swine can infect birds, as evidenced by serologic findings of cH1N1 in turkeys as well as by isolation of cH1N1, A(H1N2), and A(H3N2).[7,30,118,418,419]

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.[114] Large-scale confinement production is equivalent to that of the sector 1 poultry classification. Commonly used biosecurity measures in the production cycle of these operations include disease reporting, laboratory testing, and movement control.[26] 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.[26]

Smaller swine production is similar to that of the poultry sector 4 classification. These producers are common in rural and semi-urban areas in Asia, Central America, and Africa. Their animals are primarily raised for household consumption or sale in local markets; the swine are not transported during growth cycles, feed by scavenging, and are integral to subsistence farmers.[393] 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.[393]

The third production system is primarily in Europe where there is a unique sector of niche growers using organic production and traditional breeds. This market has the same biosecurity vulnerability as large-scale producers.[149]

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.[26]

Prevention and Control

The core tenants of influenza control among swine include facility management, herd health management and biosecurity measures, and vaccination.[411]

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 living cells for fewer than 2 weeks, except in fresh water at appropriate temperatures.[26,161] Temperature control is also important because the virus is more stable in colder temperatures. Herd management may include avoiding introduction of pigs carrying the virus for at least 3 months without quarantine.[410]

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 (Swine Influenza Epidemiology) in

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circulating SIV subtypes. The need for rapidly updated, effective vaccines becomes more critical as new triple 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 fewer than half of the 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.[410,411]

Prevention Against Infection and Illness in Humans

CDC and USDA provide extensive guidance: CDC Interim Guidance for Workers who are Employed at Commercial Swine Farms: Preventing the Spread of Influenza A Viruses | CDC.

CDC emphasizes people who work with swine should be familiar with signs of flu illness in pigs, which can include the following[324]:

- Fever
- Lethargy
- Poor appetite
- Coughing
- Discharge from nose or eyes
- Sneezing
- Difficulty breathing

With the detection of these signs, prevention measures should be implemented.

Basic prevention control guidelines

CDC emphasizes the importance of using basic prevention and control guidelines with swine workers to reduce the risk of spreading swine flu from pigs to people and also people to pigs.[324] Guidelines include the following:

- Workers should utilize PPE. A list of recommended PPE is located at this webpage: Workers Employed at Commercial Swine Farms
- Hand hygiene after contact with animals is critical as well as avoiding contact with a worker's own nose, eyes, or mouth while working with pigs.
- Vaccination of pigs is effective in reducing the risk of influenza infection in pigs, but it may not be effective as there are many co-circulating strains among pig populations.
- Consideration of the use of respirators may be needed. Guidance for this is located at the following 2 websites:
  - eTool : Respiratory Protection | Occupational Safety and Health Administration (osha.gov)
  - Respirators | NIOSH | CDC
- Seasonal influenza vaccination is recommended for swine workers to reduce the potential for co-infection with a seasonal and swine virus.

Preventing the spread of seasonal influenza from workers to pigs

Seasonal influenza can be transmitted from sick people to pigs. While rare, it is essential to reduce the risk of spread as pigs can serve as hosts for multiple types and strains of flu viruses, allowing for possible genetic reassortment under the right conditions. Workers should be able to recognize the symptoms of influenza illness and remain out of contact with other workers and pigs. If a sick worker is essential to the swine operation, extensive PPE should be used throughout the duration of that worker's illness.[324] Additional guidance is provided in the OSHA FactSheet, PPE.

Exposures to swine flu include other persons interacting with swine on farms, people attending local and state fairs who are also interacting with swine, and potentially swine processing workers; risk is reduced for this latter group, as PPE is typically required.[67,242]

Equine Influenza Surveillance, Epidemiology, Prevention, & Control

Surveillance

Equine influenza is a WOAH-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.[396]

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), although only A(H3N8) has been identified as a cause of infection in equid for more than 10 years.[267,396] Similar to influenza illness

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in humans, horses can spread infection before displaying clinical signs of illness. The virus is spread on contaminated clothing and equipment as well as between horses. International movement of horses poses a risk for virus introduction into the country of entry; however, most countries have strict import standards that include testing and quarantine on arrival.[396]

Equine influenza cases and outbreaks happen regularly throughout the world. The largest outbreak in the past 10 years occurred in Mongolia in 2011, in which more than 75,000 cases of A(H3N8) were reported.[3,267] Mongolian free-range horse herds are affected by large-scale outbreaks approximately every 10 years, leading to a significant negative economic impact.[267] South and Central America have experienced consistent outbreaks during the last 10 years. Europe and Asia (except Mongolia) regularly report sporadic cases and small outbreaks. The United States reported an outbreak among wild horses and burros in 2021.[280]

Vaccination

Equine influenza vaccination is common in many countries, but like the challenge posed by 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 WOAH convenes an expert panel at least annually to review surveillance data and make recommendations for vaccine composition.[420]

Additional Resources

- Equine Influenza: A Comprehensive Review from Etiology to Treatment - PubMed
- Equine Influenza | AAEP

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

Surveillance and Epidemiology

Results from surveillance for 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 (WOAH). 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.[421] Since then sporadic outbreaks have occurred, most recently in 2017 and 2021 among shelter dogs and in boarding, grooming, and daycare facilities in Los Angeles County, California.[291,303] CIV was considered enzootic in Colorado, New Jersey, New York, Florida, and Pennsylvania, but CIV A(H3N8) has not been detected for more than 2 years, suggesting that it may have been eliminated.[87,422] Occasional CIV studies are funded by USDA.[423]

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 and involved 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.[310]

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.[314-316] Examples of these animals include harbor seals, songbirds, parakeets, and pandas.[24,178,424] 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 that were believed to have been infected with A(H5N8) from the swans.[216]

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; see How NNDSS Conducts Case Surveillance.

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Risk Assessment

CIV is not actively circulating in US canine populations, but persistent outbreaks could result in CIV becoming endemic. 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

Canine vaccinations are available for the A(H3N8) and A(H3N2) subtypes separately and in bivalent formulation. Vaccination can reduce the risk of infection, severe illness, and death in these animals, but it may not prevent infection.

Additional Resources

- Canine Influenza - CFSPH (iastate.edu)
- Canine Influenza FAQ | American Veterinary Medical Association (avma.org)
- Canine Influenza (iastate.edu)
- Influenza (iastate.edu)
- Key Facts About Canine Influenza (Dog Flu) | Seasonal Influenza (Flu) | CDC
- Influenza in Cats | Seasonal Influenza (Flu) | CDC

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Future Considerations for Zoonotic Influenza

In the United States in 2022, widespread detection of avian influenza in wild, migratory birds led to the largest 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 detection of avian influenza in humans was confirmed in the United States in Colorado in a person with known contact with infected birds. While not an immediate threat, the prevalence of avian influenza in the United States 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; and other infectious diseases.[426-430] These events are increasing in frequency, diversity of pathogen type, global distribution of vectors and hosts, and new animal species.

If lessons are to be learned from the COVID-19 pandemic, early detection of a new viral respiratory pathogen and subsequent mitigation efforts are critical to reducing the impact on human and animal populations. In addition, a highly infectious, airborne virus will spread dramatically faster than anticipated, and the impact of public health interventions may need to be communicated quickly and frequently. The dynamic nature of how influenza viruses move through populations of animals, whether seasonally or in their acquisition of new genes, places influenza at or near the top of known diseases continually posing a threat to human and animal health.[427] An 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 diseases. Strengthening the U.S. and international public health systems is necessary to ensure the health and safety of current and future humans and animals.

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General Influenza Public Health Resources

General Influenza

- Pandemic Influenza (Flu)|CDC
- Influenza (Flu)|CDC
- Weekly US Influenza Surveillance Report
- Understanding Flu Viruses
- 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
- Issues for Fair Organizers to Consider When Planning Fairs | CDC
- 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

- CDC Interim Guidance for Workers who are Employed at Commercial Swine Farms: Preventing the Spread of Influenza A Viruses | CDC
- 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 Public Health 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[431]
- Take Action to Prevent the Spread of Flu Between Pigs and People

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)[432]
- SHIC-factsheet-influenza-cd-27Sept2021.pdf (swinehealth.org)
- A Review of Optimal Use of Diagnostics and Vaccines for Control of Influenza A Virus Infection in Swine—veterinarian handout (iastate.edu)

Avian Influenza

- Information on Avian Influenza
- Avian Influenza in Birds
- Avian Influenza A Virus Infections in Humans

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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: Stop Avian Influenza Outbreaks
- The HPAI Indemnity and Compensation Process
- Appraisal and Compensation
- 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 Organization for Animal Health (WOAH)
- 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
- American Horse Council Microchip Look-Up
- 2016 NIAA/USAHA Equine Disease 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

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Appendix A: Contact List

CDC Influenza Division

The CDC Influenza Division has an emergency contact line staffed 24/7: CDC Influenza Division: 404-639-3747. Additional contacts include CDC INFO on website: Contact CDC-INFO; 800-CDC-INFO (800-232-4636), and TTY: 888-232-6348.

National Veterinary Services Laboratories

(U.S. Department of Agriculture [USDA] Animal and Plant Health Inspection Service [APHIS] District Offices)

The Diagnostic Virology Laboratory (DVL) performs confirmatory and diagnostic testing for many domestic and foreign animal viral diseases, such as vesicular stomatitis (VS), highly pathogenic avian influenza (HPAI), virulent Newcastle disease, equine encephalomyelitis viruses (e.g., Eastern equine encephalomyelitis [EEE]), equine infectious anemia (EIA), bluetongue (BT), swine influenza, pseudorabies (PRV), and West Nile encephalitis. Maintaining expertise for these diseases and other viral agents is part of DVL's role in protecting the American livestock industry.

Email contact (including urgent/after-hours) and mailing information:
USDA APHIS | NVSL Diagnostic Virology Laboratory.

Phone numbers:

NVSL FADDL	
Main Office	(631) 323-3256
AFTER HOURS AND WEEKENDS	
Diagnostic Services Section Head	(631) 375-5314
Acting Diagnostic Services Section Head	(631) 405-0218
Courier	(631) 566-0073

NVSL AMES	
NVSL Director	(515) 337-7601
Diagnostic Virology	(515) 337-7551
Diagnostic Bacteriology & Pathology	(515) 337-7526
Diagnostic Bioanalytical & Reagent	(515) 337-7563
AFTER HOURS AND WEEKENDS	
Nat'l Centers for Animal Health Dispatch	(515) 337-7200

NPIC (M-F, 8:00 AM – 4:30 PM ET)	
Jon Zack	(240) 252-8074
Barbara Porter-Spalding	(919) 637-4409
AFTER HOURS AND WEEKENDS	
NPIC/NVS 24/7 Emergency Answering Service	(800) 940-6524

APHIS VS DISTRICT OFFICES	
District One	(508) 363-2290
District Two	(517) 337-4700
District Three	(916) 854-3950
District Four	(512) 383-2400

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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://www.cste.org/page/EpiOnCall

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 (WOAH)

Professional Organizations

- American Veterinary Medical Association (AVMA)
- Association of American Veterinary Medical Colleges (AAVMC)
- Pet Advocacy Network (previously known as 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

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References

1. USDA. USDA APHIS | 2017 Highly Pathogenic Avian Influenza. Updated 2017.
2. CDC. FluView. Updated 2021. https://www.cdc.gov/flu/weekly/fluactivitysurv.htm
3. WOAH. WOAH-WAHIS International Animal Disease Dashboard. Updated 2021. https://wahis.woah.org/#/home
4. CDC. Influenza Virus Genome Sequencing and Genetic Characterization. Updated 2021-11-02. https://www.cdc.gov/flu/about/professionals/genetic-characterization.htm
5. Jianzhong Shi XZ, Pengfei Cui, Cheng Yan, and Hualan Chena. Alarming situation of emerging H5 and H7 avian influenza and effective control strategies. *Emerging Microbes & Infections*. 12/12/2022 2023;v.12(1)
6. Gao F, Yang J, Pan J, Liang X. Frontiers | Origin and Evolution of H1N1/pdm2009: A Codon Usage Perspective. *Frontiers in Microbiology*. 2020;11doi:doi:10.3389/fmicb.2020.01615
7. Mostafa A, Abdelwhab E, Mettenleiter T, Pleschka S. Zoonotic Potential of Influenza A Viruses: A Comprehensive Overview. *Viruses*. 2018-09-13 2018;10(9):497. doi:10.3390/v10090497
8. Widdowson M-A, Bresee JS, Jernigan DB. The Global Threat of Animal Influenza Viruses of Zoonotic Concern: Then and Now. *The Journal of Infectious Diseases*. 2017-09-15 2017;216(suppl_4):S493-S498. doi:10.1093/infdis/jix331
9. Anne Günther1 OK, Vilhjalmur Svansson1, Anne Pohlmann, Jacqueline King, Gunnar Thor Hallgrimsson, Kristinn Haukur Skarphéðinsson, Heiða Sigurðardóttir, Stefán Ragnar Jónsson, Martin Beer, Brigitte Brugger, and Timm Harder. Iceland as Stepping Stone for Spread of Highly Pathogenic Avian Influenza Virus between Europe and North America - Volume 28, Number 12—December 2022 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. November 21, 2022 2022;doi:10.3201/eid2812.221086
10. Bouvier NM, Palese P. The Biology of Influenza Viruses. *Vaccine*. 2008-9-12 2008;26(Suppl 4):D49-D53.
11. CDC. Types of Influenza Viruses. Updated 2021-11-02. https://www.cdc.gov/flu/about/viruses/types.htm
12. Olsen B, Munster VJ, Wallensten A, Waldenström J, Osterhaus ADME, Fouchier RAM. Global Patterns of Influenza A Virus in Wild Birds. *Science*. 2006-04-21 2006;312(5772):384-388. doi:10.1126/science.1122438
13. CDC. Influenza Type A Viruses. Updated 2020-02-10T04:05:16Z. https://www.cdc.gov/flu/about/viruses/types.htm
14. CDC. Novel Influenza A Virus Infections. Updated 2021. https://gis.cdc.gov/grasp/fluview/Novel_Influenza.html
15. Survey USG. Avian Influenza. Updated 7/24/2018. https://www.usgs.gov/centers/national-wildlife-health-center/science/science-topics/avian-influenza
16. Abolnik C, Londt BZ, Manvell RJ, et al. Characterisation of a highly pathogenic influenza A virus of subtype H5N2 isolated from ostriches in South Africa in 2004. *Influenza and Other Respiratory Viruses*. 2009-3 2009;3(2):63-68. doi:10.1111/j.1750-2659.2009.00074.x
17. Bodewes R, Morick D, Mutsert Gd, et al. Recurring Influenza B Virus Infections in Seals. *Emerging Infectious Diseases*. 3/2013 2013;doi:10.3201/eid1903.120965

18. CDC. Outbreaks of Avian Influenza A (H5N2), (H5N8), and (H5N1) Among Birds — United States, December 2014–January 2015. Updated 2/2015. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6404a9.htm?s_cid=mm6404a9_w
19. CDC. Bat Influenza (Flu) | Seasonal Influenza (Flu). Updated 2018-09-27T12:54:10Z/. https://www.cdc.gov/flu/other/bat-flu.html
20. CDC. Influenza A Subtypes and the Species Affected | Seasonal Influenza (Flu). Updated 2018-09-27T12:55:28Z/. https://www.cdc.gov/flu/other/animal-flu.html
21. CDC. Influenza in Animals. Updated 2018-09-27. https://www.cdc.gov/flu/other/index.html
22. CDC. Key Facts about Canine Influenza (Dog Flu) | Seasonal Influenza (Flu). Updated 2018-09-27T12:56:00Z/. https://www.cdc.gov/flu/other/canine-flu/keyfacts.html
23. CDC. Key Facts about Swine Influenza (Swine Flu) in Pigs | CDC. Updated 2018-10-03T12:22:22Z. https://www.cdc.gov/flu/swineflu/keyfacts_pigs.htm
24. Martelli P, Teng JLL, Lee F-K, et al. Influenza A(H1N1)pdm09 Virus Infection in a Captive Giant Panda, Hong Kong. *Emerging Infectious Diseases journal*. December 2019 2019;25(12) doi:10.3201/eid2512.191143
25. Osterhaus AD, Rimmelzwaan GF, Martina BE, Bestebroer TM, Fouchier RA. Influenza B virus in seals. *Science (New York, NY)*. 2000-05-12 2000;288(5468):1051-1053. doi:10.1126/science.288.5468.1051
26. Swayne DE. Animal Influenza. Wiley. Updated 2017. https://onlinelibrary.wiley.com/doi/book/10.1002/9781118924341
27. Taubenberger JK, Kash JC. Influenza Virus Evolution, Host Adaptation and Pandemic Formation. *Cell host & microbe*. 2010-6-25 2010;7(6):440-451. doi:10.1016/j.chom.2010.05.009
28. Taubenberger JK, Morens DM. The Pathology of Influenza Virus Infections. *Annual review of pathology*. 2008 2008;3:499-522. doi:10.1146/annurev.pathmechdis.3.121806.154316
29. Olsen CW. The emergence of novel swine influenza viruses in North America. *Virus Research*. May 10, 2002 2002;85(2):199-210. doi:10.1016/S0168-1702(02)00027-8
30. Webster RG, Bean WJ, Gorman OT, Chambers TM, Kawaoka Y. Evolution and ecology of influenza A viruses. *Microbiological Reviews*. 1992-3 1992;56(1):152-179.
31. CDC. Past Pandemics | Pandemic Influenza (Flu). Updated 2019-06-11T03:41:20Z/. https://www.cdc.gov/flu/pandemic-resources/basics/past-pandemics.html
32. Nelson MI, Gramer MR, Vincent AL, Holmes EC. Global transmission of influenza viruses from humans to swine. *The Journal of General Virology*. October 2012 2012;93(Pt 10):2195. doi:10.1099/vir.0.044974-0
33. Virk RK, Jayakumar J, Mendenhall IH, et al. Divergent evolutionary trajectories of influenza B viruses underlie their contemporaneous epidemic activity. *Proceedings of the National Academy of Sciences*. 2020/01/07 2020;117(1):619-628. doi:10.1073/pnas.1916585116
34. Hause BM, Ducatez M, Collin EA, et al. Isolation of a Novel Swine Influenza Virus from Oklahoma in 2011 Which Is Distantly Related to Human Influenza C Viruses. *PLoS Pathogens*. 2013-2-7 2013;9(2):e1003176. doi:10.1371/journal.ppat.1003176
35. Zhou NN, Senne DA, Landgraf JS, et al. Genetic reassortment of avian, swine, and human influenza A viruses in American pigs. *Journal of Virology*. 1999-10 1999;73(10):8851-8856. doi:10.1128/JVI.73.10.8851-8856.1999
36. Brown IH. The epidemiology and evolution of influenza viruses in pigs. *Veterinary Microbiology*. 2000-05-22 2000;74(1-2):29-46. doi:10.1016/s0378-1135(00)00164-4
37. Garten RJ, Davis CT, Russell C, Shu B, Lindstrom S. Antigenic and Genetic Characteristics of Swine-Origin 2009 A(H1N1) Influenza Viruses Circulating in Humans. *Science*. 7/10/2009 2009;325(5937)doi:10.1126/science.1176225

38. Youzbashi E, Marschall M, Chaloupka I, Meier-Ewert H. Distribution of influenza C virus infection in dogs and pigs in Bavaria. *Tierarztliche Praxis*. 1996-08 1996;24(4):337-342.
39. Koutsakos M, Wheatley AK, Laurie K, Kent SJ, Rockman S. Influenza lineage extinction during the COVID-19 pandemic? *Nature Reviews Microbiology*. 2021-12 2021;19(12):741-742. doi:10.1038/s41579-021-00642-4
40. Kimura H, Abiko C, Peng G, et al. Interspecies transmission of influenza C virus between humans and pigs. *Virus Research*. 1997-04 1997;48(1):71-79. doi:10.1016/s0168-1702(96)01427-x
41. Zhang H, Porter E, Lohman M, et al. Influenza C Virus in Cattle with Respiratory Disease, United States, 2016–2018. *Emerging Infectious Diseases journal*. October 2018 2018;24(10) doi:10.3201/eid2410.180589
42. Homma M, Ohyama S, Katagiri S. Age Distribution of the Antibody to Type C Influenza Virus. *Microbiology and Immunology*. 1982 1982;26(7):639-642. doi:10.1111/mim.1982.26.7.639
43. Chiapponi C, Faccini S, Fusaro A, et al. Detection of a New Genetic Cluster of Influenza D Virus in Italian Cattle. *Viruses*. 2019-11-30 2019;11(12):1110. doi:10.3390/v11121110
44. Gorin S, Fablet C, Quéguiner S, et al. Assessment of Influenza D Virus in Domestic Pigs and Wild Boars in France: Apparent Limited Spread within Swine Populations Despite Serological Evidence of Breeding Sow Exposure. *Viruses*. 2019-12-24 2019;12(1):25. doi:10.3390/v12010025
45. Silveira S, Falkenberg SM, Kaplan BS, et al. Serosurvey for Influenza D Virus Exposure in Cattle, United States, 2014–2015. *Emerging Infectious Diseases*. 11/2019 2019;25(11):2074-2080. doi:10.3201/eid2511.190253
46. White SK, Ma W, McDaniel CJ, Gray GC, Lednicky JA. Serologic evidence of exposure to influenza D virus among persons with occupational contact with cattle. *Journal of Clinical Virology: The Official Publication of the Pan American Society for Clinical Virology*. 2016-08 2016;81:31-33. doi:10.1016/j.jcv.2016.05.017
47. Sederdahl BK, Williams JV. Epidemiology and Clinical Characteristics of Influenza C Virus. *Viruses*. 2020-1-13 2020;12(1):89. doi:10.3390/v12010089
48. WHO. Influenza Nomenclature. *Weekly Epidemiological Record*. 9/1980 1980;
49. WHO. Standardization of terminology of the pandemic A(H1N1) 2009 virus. *Weekly Epidemiological Record*. 10/2011 2011;
50. CDC. AMD: Enhancing Surveillance | Advanced Molecular Detection. Updated 2019-10-11T06:46:42Z. https://www.cdc.gov/amd/what-we-do/surveillance.html
51. WHO. Global Influenza Strategy 2019-2030. Updated 2019. https://www.who.int/publications-detail-redirect/9789241515320
52. Kapoor S, Dhama, Kuldeep. *Insight into Influenza Viruses of Animals and Humans*. Springer; 2014.
53. Childs J, Mackenzie J, Richt J. *Wildlife and Emerging Zoonotic Diseases: The Biology, Circumstances and Consequences of Cross-Species Transmission*. 2007.
54. Compans R. *Influenza Pathogenesis and Control - Volume I*. Springer; 2014.
55. Paget J, Spreeuwenberg P, Charu V, et al. Global mortality associated with seasonal influenza epidemics: New burden estimates and predictors from the GLaMOR Project. *Journal of Global Health*. 12/2019 2019;9(2):020421. doi:10.7189/jogh.09.020421
56. CDC. Burden of Influenza. Updated 2021-10-04. https://www.cdc.gov/flu/about/burden/index.html
57. WHO. Influenza (Seasonal). Updated 11/6/2018. https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)
58. CDC. Key Facts About Influenza (Flu). Updated 2021-08-26T08:46:12Z. https://www.cdc.gov/flu/about/keyfacts.htm

59. Nguyen-Van-Tam JS, Hampson AW. The epidemiology and clinical impact of pandemic influenza. *Vaccine*. 2003-05-01 2003;21(16):1762-1768. doi:10.1016/s0264-410x(03)00069-0

60. CDC. How to Prevent Flu. Updated 2021-10-25. https://www.cdc.gov/flu/prevent/index.html

61. CDC. Flu Symptoms & Complications. Updated 2021-09-21. https://www.cdc.gov/flu/symptoms/symptoms.htm

62. CDC. People at High Risk of Flu. Updated 2021-10-12. https://www.cdc.gov/flu/highrisk/index.htm

63. CDC. Selecting Viruses for the Seasonal Flu Vaccine. Updated 2021-08-31. https://www.cdc.gov/flu/prevent/vaccine-selection.htm

64. Weir JP. *Influenza Virus Vaccine Strain Selection 2021-2022 Northern Hemisphere*. 2021:8. 3/5/2021. https://www.fda.gov/media/146448/download

65. CDC. What You Should Know about Flu Antiviral Drugs. Updated 2021-08-31. https://www.cdc.gov/flu/pdf/freeresources/updated/What-you-Should-Know-About-Flu-Antiviral-Drug2022s.pdf

66. Sutton TC. The Pandemic Threat of Emerging H5 and H7 Avian Influenza Viruses. *Viruses*. 2018-8-28 2018;10(9):461. doi:10.3390/v10090461

67. CDC. Swine Influenza (Influenza in Swine) | CDC. Updated 2018-11-09T01:08:36Z. https://www.cdc.gov/flu/swineflu/index.htm

68. CDC. Key Facts about Human Infections with Variant Viruses. Updated 2019-01-03T06:47:44Z. https://www.cdc.gov/flu/swineflu/keyfacts-variant.htm

69. CDC. Viruses of Special Concern. Updated 2019-05-07T04:38:00Z/. https://www.cdc.gov/flu/weekly/index.htm#ILIMap

70. WHO. World Health Organization (WHO) Pandemic Definition - Public Health. Updated 2021-04-19T16:44:18+00:00. https://www.publichealth.com.ng/world-health-organization-who-pandemic-definition/

71. CDC. Section 11: Epidemic Disease Occurrence. https://archive.cdc.gov/#/details?url=https://www.cdc.gov/csels/dsepd/ss1978/lesson1/section11.html

72. Glezen WP. Emerging Infections: Pandemic Influenza. *Epidemiologic Reviews*. 1996-01-01 1996;18(1):64-76. doi:10.1093/oxfordjournals.epirev.a017917

73. CDC. 1957-1958 Pandemic (H2N2 virus) | Pandemic Influenza (Flu). Updated 2019-01-22T09:08:45Z. https://archive.cdc.gov/#/details?url=https://www.cdc.gov/flu/pandemic-resources/1957-1958-pandemic.html

74. CDC. 1968 Pandemic (H3N2 virus) | Pandemic Influenza (Flu). Updated 2019-01-22T09:09:30Z. https://archive.cdc.gov/#/details?url=https://www.cdc.gov/flu/pandemic-resources/1968-pandemic.html

75. CDC. 2009 H1N1 Pandemic. Updated 2019-06-11.https://archive.cdc.gov/#/details?url=https://www.cdc.gov/flu/pandemic-resources/2009-h1n1-pandemic.html

76. CDC. 1918 Pandemic (H1N1 virus) | Pandemic Influenza (Flu). Updated 2020-06-16T05:25:33Z. https://archive.cdc.gov/#/details?url=https://www.cdc.gov/flu/pandemic-resources/1918-pandemic-h1n1.html

77. Gaydos JC, Top FH, Hodder RA, Russell PK. Swine Influenza A Outbreak, Fort Dix, New Jersey, 1976 - Volume 12, Number 1—January 2006 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. 2006;doi:10.3201/eid1201.050965

78. Kilbourne ED. Influenza Pandemics of the 20th Century. *Emerging Infectious Diseases*. 2006-1 2006;12(1):9-14. doi:10.3201/eid1201.051254

79. Scholtissek C, von Hoyningen V, Rott R. Genetic relatedness between the new 1977 epidemic strains (H1N1) of influenza and human influenza strains isolated between 1947 and 1957 (H1N1). *Virology*. 1978-09 1978;89(2):613-617. doi:10.1016/0042-6822(78)90203-9

80. Crosby AW. *America's Forgotten Pandemic: The Influenza of 1918*. 2 ed. Cambridge University Press; 2003.

81. Young A. Equine influenza (flu). UC Davis. Updated 2019-07-08T11:09:19-07:00. https://ceh.vetmed.ucdavis.edu/health-topics/equine-influenza-flu

82. Worobey M, Han G-Z, Rambaut A. A synchronized global sweep of the internal genes of modern avian influenza virus. *Nature*. 2014-4-10 2014;508(7495):254-257. doi:10.1038/nature13016

83. Zimmer SM, Burke DS. Historical Perspective — Emergence of Influenza A (H1N1) Viruses. *New England Journal of Medicine*. July 16, 2009 2009;361(3):279-285. doi:10.1056/NEJMra0904322

84. Marks JS, Halpin TJ. Guillain-Barré Syndrome in Recipients of A/New Jersey Influenza Vaccine. *JAMA*. June 27, 1980 1980;243(24):2490-2494. doi:10.1001/jama.1980.03300500016019

85. Lessler J, Cummings DAT, Fishman S, Vora A, Burke DS. Transmissibility of swine flu at Fort Dix, 1976. *Journal of the Royal Society Interface*. 2007-8-22 2007;4(15):755-762. doi:10.1098/rsif.2007.0228

86. Fouchier R. Animal influenza virus surveillance. *Vaccine*. 2003-05-01 2003;21(16):1754-1757. doi:10.1016/S0264-410X(03)00067-7

87. Kile J. Interview and notes provided by Dr. James Kile. 2022.

88. Dawood FS, Jain S, Finelli L. Emergence of a Novel Swine-Origin Influenza A (H1N1) Virus in Humans. *New England Journal of Medicine*. 2009-06-18 2009;360(25):2605-2615. doi:10.1056/NEJMoa0903810

89. Kendal AP, Noble GR, Skehel JJ, Dowdle WR. Antigenic similarity of influenza A (H1N1) viruses from epidemics in 1977--1978 to "Scandinavian" strains isolated in epidemics of 1950--1951. *Virology*. 1978-09 1978;89(2):632-636. doi:10.1016/0042-6822(78)90207-6

90. Rozo M, Gronvall GK. The Reemergent 1977 H1N1 Strain and the Gain-of-Function Debate. *mBio*. 2015-8-18 2015;6(4):e01013-15. doi:10.1128/mBio.01013-15

91. Wertheim JO. The Re-Emergence of H1N1 Influenza Virus in 1977: A Cautionary Tale for Estimating Divergence Times Using Biologically Unrealistic Sampling Dates. *PLOS ONE*. Jun 17, 2010 2010;5(6):e11184. doi:10.1371/journal.pone.0011184

92. Garten RJ, Davis CT, Russell CA, et al. Antigenic and Genetic Characteristics of the Early Isolates of Swine-Origin 2009 A(H1N1) Influenza Viruses Circulating in Humans. *Science (New York, NY)*. 2009-7-10 2009;325(5937):197-201. doi:10.1126/science.1176225

93. Swerdlow DL, Finelli L, Bridges C. The 2009 H1N1 Influenza Pandemic: Field and Epidemiologic Investigations. *Clinical Infectious Diseases*. 2011-01-01 2011;52(suppl_1):NP-NP. doi:10.1093/cid/ciq062

94. CDC. 2009 H1N1 Pandemic (H1N1pdm09 virus) | Pandemic Influenza (Flu) | CDC. @CDCgov. Updated 2023-05-16T01:46:06Z. https://www.cdc.gov/flu/pandemic-resources/2009-h1n1-pandemic.html

95. Mena I, Nelson MI, Quezada-Monroy F, et al. Origins of the 2009 H1N1 influenza pandemic in swine in Mexico. *eLife Sciences Publications Limited*. 2016-06-28 2016;doi:doi:10.7554/eLife.16777

96. Goneau L, Mehta K, Wong J, L'Huillier A, Gubbay J. Zoonotic Influenza and Human Health—Part 1: Virology and Epidemiology of Zoonotic Influenzas. *Current Infectious Disease Reports*. 10/2018 2018;20(10):37. doi:10.1007/s11908-018-0642-9

97. CDC. Specific Variant Flu Viruses | CDC. Updated 2020-01-29T07:13:28Z. https://www.cdc.gov/flu/other/index.html

98. CDC. Situation Summary on Influenza A (H3N2) Variant Viruses ("H3N2v"). Updated 2020-01-29T08:44:20Z. https://www.cdc.gov/flu/swineflu/variant-flu-in-humans.htm

99. Claas EC, Osterhaus AD, van Beek R, et al. Human influenza A H5N1 virus related to a highly pathogenic avian influenza virus. *Lancet (London, England)*. 1998-02-14 1998;351(9101):472-477. doi:10.1016/S0140-6736(97)11212-0

100. USDA. USDA APHIS | Highly Pathogenic Avian Influenza (HPAI). Updated 2022.

101. WHO. Global Influenza Surveillance and Response System (GISRS). Updated 2021. https://www.who.int/initiatives/global-influenza-surveillance-and-response-system

102. WOAH. Who we are. *WOAH - World Organisation for Animal Health* blog. 2021. Accessed 2021-12-17 04:30:46. https://www.woah.org/en/who-we-are/

103. CDC. CDC's One Health Office: What We Do. Updated 2020-02-27T08:24:46Z. https://www.cdc.gov/onehealth/what-we-do/index.html

104. CDC. CDC's One Health Office: Who We Are. Updated 2020-02-18T05:52:04Z. https://www.cdc.gov/onehealth/what-we-do/index.html

105. Greene JL. *Update on the Highly-Pathogenic Avian Influenza Outbreak of 2014-2015*. 2015:18. 2015. https://sgp.fas.org/crs/misc/R44114.pdf

106. He G, Ming L, Li X, et al. Early Release - Genetically Divergent Highly Pathogenic Avian Influenza A(H5N8) Viruses in Wild Birds, Eastern China - Volume 27, Number 11—November 2021 - Emerging Infectious Diseases journal - CDC. *Emerging Infectious Diseases*. 11/2021 2021;doi:10.3201/eid2711.204893

107. Smyth GB, Dagley K, Tainsh J. Insights into the economic consequences of the 2007 equine influenza outbreak in Australia. *Australian Veterinary Journal*. 2011-07 2011;89 Suppl 1:151-158. doi:10.1111/j.1751-0813.2011.00777.x

108. Venter M, Treurnicht FK, Buys A, et al. Risk of Human Infections With Highly Pathogenic H5N2 and Low Pathogenic H7N1 Avian Influenza Strains During Outbreaks in Ostriches in South Africa. *The Journal of infectious diseases*. 2017-9-15 2017;216(Suppl 4):S512-S519. doi:10.1093/infdis/jix018

109. CDC. Influenza Risk Assessment Tool (IRAT) | Pandemic Influenza (Flu). Updated 2020-11-27T04:01:28Z. https://www.cdc.gov/pandemic-flu/php/national-strategy/influenza-risk-assessment-tool.html

110. CDC. Influenza Risk Assessment Tool Results. Updated 2021-12-02. https://www.cdc.gov/flu/pandemic-resources/monitoring/irat-virus-summaries.htm

111. CDC. CDC's World Health Organization Collaborating Center. Updated 2021-11-17. https://www.cdc.gov/flu/weekly/who-collaboration.htm

112. Becker WB. The isolation and classification of Tern virus: influenza A-Tern South Africa--1961. *The Journal of Hygiene*. 1966-9 1966;64(3):309-320. doi: https://doi.org/10.1017%2Fs0022172400040596

113. Latorre-Margalef N, Gunnarsson G, Munster VJ, et al. Effects of influenza A virus infection on migrating mallard ducks. *Proceedings of the Royal Society B: Biological Sciences*. 2009-3-22 2009;276(1659):1029-1036. doi:10.1098/rspb.2008.1501

114. FAO, WOAH, WHO. A Global Strategy for the Progressive Control of Highly Pathogenic Avian Influenza (HPAI). Updated 11/2005. https://www.semanticscholar.org/paper/A-global-strategy-for-the-progressive-control-of-Oie/366fac12e92129b3833b0bc5979bac944e291aea

115. Costa T, Chaves AJ, Valle R, et al. Distribution patterns of influenza virus receptors and viral attachment patterns in the respiratory and intestinal tracts of seven avian species. *Veterinary Research*. 2012-04-10 2012;43:28. doi:10.1186/1297-9716-43-28

116. Perez DR, Lim W, Seiler JP, et al. Role of Quail in the Interspecies Transmission of H9 Influenza A Viruses: Molecular Changes on HA That Correspond to Adaptation from Ducks to Chickens. *Journal of Virology*. March 2003 2003;77(5):3148. doi:10.1128/JVI.77.5.3148-3156.2003

117. Banks J, Speidel E, Alexander DJ. Characterisation of an avian influenza A virus isolated from a human--is an intermediate host necessary for the emergence of pandemic influenza viruses? *Archives of Virology*. 1998 1998;143(4):781-787. doi:10.1007/s007050050329

118. Choi YK, Lee JH, Erickson G, et al. H3N2 Influenza Virus Transmission from Swine to Turkeys, United States. *Emerging Infectious Diseases*. 12/2004 2004;doi:10.3201/eid1012.040581

119. Nakayama M, Uchida Y, Shibata A, et al. A novel H7N3 reassortant originating from the zoonotic H7N9 highly pathogenic avian influenza viruses that has adapted to ducks. *Transboundary & Emerging Diseases*. November 2019 2019;66(6):2342-2352. doi:10.1111/tbed.13291

120. Tsukamoto K, Imada T, Tanimura N, et al. Impact of different husbandry conditions on contact and airborne transmission of H5N1 highly pathogenic avian influenza virus to chickens. *Avian Diseases*. 2007-03 2007;51(1):129-132. doi:10.1637/0005-2086(2007)051[0129:IODHCO]2.0.CO;2

121. Zhou J, Wu J, Zeng X, et al. Isolation of H5N6, H7N9 and H9N2 avian influenza A viruses from air sampled at live poultry markets in China, 2014 and 2015. *Euro Surveillance: Bulletin Europeen Sur Les Maladies Transmissibles = European Communicable Disease Bulletin*. 2016-09-01 2016;21(35)doi:10.2807/1560-7917.ES.2016.21.35.30331

122. Organization WH. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2023. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/cumulative-number-of--confirmed-human-cases-for-avian-influenza-a(h5n1)-reported-to-who--2003-2023.pdf?sfvrsn=c6600b55_1&download=true

123. Kreijtz JHCM, Kroeze EJBV, Stittelaar KJ, et al. Low pathogenic avian influenza A(H7N9) virus causes high mortality in ferrets upon intratracheal challenge: a model to study intervention strategies. *Vaccine*. 2013-10-09 2013;31(43):4995-4999. doi:10.1016/j.vaccine.2013.06.071

124. Swayne DE. Avian Influenza - Poultry. https://www.merckvetmanual.com/poultry/avian-influenza/avian-influenza

125. WHO. Influenza at the human-animal interface summary and assessment, April 2021. Updated 4/2021. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_may_2021.pdf?sfvrsn=d75e4b5c_7&download=true

126. Root JJ. What Are the Transmission Mechanisms of Influenza A Viruses in Wild Mammals? *The Journal of Infectious Diseases*. 2020-01-02 2020;221(2):169-171. doi:10.1093/infdis/jiz033

127. Gu M, Chen H, Li Q, et al. Enzootic genotype S of H9N2 avian influenza viruses donates internal genes to emerging zoonotic influenza viruses in China. *Veterinary Microbiology*. 12/2014 2014;174(3-4):309-315. doi:10.1016/j.vetmic.2014.09.029

128. Mutinelli F, Capua I, Terregino C, Cattoli G. Clinical, Gross, and Microscopic Findings in Different Avian Species Naturally Infected during the H7N1 Low- and High-Pathogenicity Avian Influenza Epidemics in Italy during 1999 and 2000. *Avian Diseases*. 2003 2003;47:844-848.

129. USDA. Epidemiologic and Other Analyses of HPAI-Affected Poultry Flocks, 2014-2015. Updated 2014. https://www.aphis.usda.gov/animal_health/animal_dis_spec/poultry/downloads/Epidemiologic-Analysis-Sept-2015.pdf

130. Pasick J, Berhane Y, Joseph T, et al. Reassortant Highly Pathogenic Influenza A H5N2 Virus Containing Gene Segments Related to Eurasian H5N8 in British Columbia, Canada, 2014. *Scientific Reports*. 2015 2015;5doi:10.1038/srep09484

131. Hillel O. Nature in Movement: Bird Flyways as Engines of Economic Growth and Conservation for City Managers. *The Nature of Cities* blog. 2013. Accessed 2022-01-23 01:22:01. https://www.thenatureofcities.com/2013/07/26/nature-in-movement-bird-flyways-as-engines-of-economic-growth-and-conservation-for-city-managers/

132. USGS, APHIS U, System NWR, Council NF. Early Detection and Monitoring for Avian Influenzas of Significant in Wild Birds. Updated 2015. https://www.aphis.usda.gov/animal_health/downloads/animal_diseases/ai/wild-bird-strategic-plan.pdf

133. WysInfo. Migratory Birds Without Boundaries. *WysInfo Docuwebs - Documentaries On The Web* blog. 2023. Accessed 2022-01-23 01:25:24. https://wysinfo.com/migratory-birds-without-boundaries/

134. Garcia M, Crawford J, Latimer J. Heterogeneity in the haemagglutinin gene and emergence of the highly pathogenic phenotype among recent H5N2 avian influenza viruses from Mexico. Updated 7/1/1996. https://www.microbiologyresearch.org/content/journal/jgv/10.1099/0022-1317-77-7-1493#tab2

135. WOAH. Avian Influenza: Terrestrial Manual. Updated 2021. https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-manual-online-access/

136. Pulit-Penaloza JA, Brock N, Pappas C, et al. Characterization of highly pathogenic avian influenza H5Nx viruses in the ferret model. *Scientific Reports*. 2020-7-29 2020;10:12700. doi:10.1038/s41598-020-69535-5

137. Ramey AM, Hill NJ, DeLiberto TJ, et al. Highly pathogenic avian influenza is an emerging disease threat to wild birds in North America. *The Journal of Wildlife Management*. 1/11/2022 2022;n/a(n/a)doi:10.1002/jwmg.22171

138. Spekreijse D, Bouma A, Koch G, Stegeman JA. Airborne transmission of a highly pathogenic avian influenza virus strain H5N1 between groups of chickens quantified in an experimental setting. *Veterinary Microbiology*. 2011-08-26 2011;152(1-2):88-95. doi:10.1016/j.vetmic.2011.04.024

139. Hansbro PM, Warner S, Tracey JP, et al. Surveillance and Analysis of Avian Influenza Viruses, Australia. *Emerging Infectious Diseases*. 12/2010 2010;16doi:10.3201/eid1612.100776

140. Rimondi A, Xu K, Craig MI, et al. Phylogenetic Analysis of H6 Influenza Viruses Isolated from Rosy-Billed Pochards (Netta peposaca) in Argentina Reveals the Presence of Different HA Gene Clusters ▼. *Journal of Virology*. 2011-12 2011;85(24):13354-13362. doi:10.1128/JVI.05946-11

141. Liu B, Havers FP, Zhou L, et al. Clusters of Human Infections With Avian Influenza A(H7N9) Virus in China, March 2013 to June 2015. *The Journal of Infectious Diseases*. September 15, 2017 2017;216(suppl_4):S548-S554. doi:10.1093/infdis/jix098

142. Chen Y, Liang W, Yang S, et al. Human infections with the emerging avian influenza A H7N9 virus from wet market poultry: clinical analysis and characterisation of viral genome. *Lancet (London, England)*. 2013 2013;381(9881):1916-1925. doi:10.1016/S0140-6736(13)60903-4

143. Kile JC, Ren R, Liu L, et al. Update: Increase in Human Infections with Novel Asian Lineage Avian Influenza A(H7N9) Viruses During the Fifth Epidemic — China, October 1, 2016–August 7, 2017. *MMWR Morbidity and Mortality Weekly Report*. 2017-9-08 2017;66(35):928-932. doi:10.15585/mmwr.mm6635a2

144. Yang L, Zhu W, Li X, et al. Genesis and Spread of Newly Emerged Highly Pathogenic H7N9 Avian Viruses in Mainland China. *Journal of Virology*. 2017-11-14 2017;91(23):e01277-17. doi:10.1128/JVI.01277-17

145. Iuliano AD. Increase in Human Infections with Avian Influenza A(H7N9) Virus During the Fifth Epidemic — China, October 2016–February 2017. *MMWR Morbidity and Mortality Weekly Report*. 2017 2017;66doi:10.15585/mmwr.mm6609e2

146. Ke C, Mok CKP, Zhu W, et al. Human Infection with Highly Pathogenic Avian Influenza A(H7N9) Virus, China. *Emerging Infectious Diseases*. 2017-8 2017;23(8):1332-1340. doi:10.3201/eid2308.170600

147. CDC. Asian Lineage Avian Influenza A(H7N9) Virus | Avian Influenza (Flu). Updated 2020-06-10T04:47:51Z. https://www.cdc.gov/mmwr/volumes/66/wr/mm6635a2.htm

148. Alexander DJ, Brown IH. Recent zoonoses caused by influenza A viruses. *Revue Scientifique Et Technique (International Office of Epizootics)*. 2000-04 2000;19(1):197-225. doi:10.20506/rst.19.1.1220

149. Perkins LEL, Swayne DE. Pathogenicity of a Hong Kong-Origin H5N1 Highly Pathogenic Avian Influenza Virus for Emus, Geese, Ducks, and Pigeons. *Avian Diseases*. 2002 2002;46(1):53-63.

150. Freidl GS, Meijer A, Bruin Ed, et al. Influenza at the animal–human interface: a review of the literature for virological evidence of human infection with swine or avian influenza viruses other than A(H5N1). *Eurosurveillance*. 2014/05/08 2014;19(18):20793. doi:10.2807/1560-7917.ES2014.19.18.20793

151. Basler CF, Reid AH, Dybing JK, et al. Sequence of the 1918 pandemic influenza virus nonstructural gene (NS) segment and characterization of recombinant viruses bearing the 1918 NS genes. *Proceedings of the National Academy of Sciences*. 2001-02-27 2001;98(5):2746-2751. doi:10.1073/pnas.031575198

152. Chen Y, Graf L, Chen T, et al. Rare variant MX1 alleles increase human susceptibility to zoonotic H7N9 influenza virus. *Science*. August 20, 2021 2021;373(6557):918-922. doi: https://doi.org/10.1126/science.abg5953

153. Alexander DJ. Summary of Avian Influenza Activity in Europe, Asia, Africa, and Australasia, 2002–2006. *Avian Diseases*. 2007/03 2007;51(s1):161-166. doi:10.1637/7602-041306R.1

154. Marchenko VY, Susloparov IM, Kolosova NP, et al. Influenza A(H5N8) virus isolation in Russia, 2014. *Archives of Virology*. 2015-11 2015;160(11):2857-2860. doi:10.1007/s00705-015-2570-4

155. Marinova-Petkova A, Georgiev G, Seiler P, et al. Spread of influenza virus A (H5N1) clade 2.3.2.1 to Bulgaria in common buzzards. *Emerging Infectious Diseases*. 2012-10 2012;18(10):1596-1602. doi:10.3201/eid1810.120357

156. Sakoda Y, Ito H, Uchida Y, et al. Reintroduction of H5N1 highly pathogenic avian influenza virus by migratory water birds, causing poultry outbreaks in the 2010-2011 winter season in Japan. *The Journal of General Virology*. 2012-03 2012;93(Pt 3):541-550. doi:10.1099/vir.0.037572-0

157. Smith GJD, Donis RO, Group WHOWOfAHFaAOWOFHEW. Nomenclature updates resulting from the evolution of avian influenza A(H5) virus clades 2.1.3.2a, 2.2.1, and 2.3.4 during 2013-2014. *Influenza and Other Respiratory Viruses*. 2015-09 2015;9(5):271-276. doi:10.1111/irv.12324

158. Kwon J-H, Noh YK, Lee D-H, et al. Experimental infection with highly pathogenic H5N8 avian influenza viruses in the Mandarin duck (Aix galericulata) and domestic pigeon (Columba livia domestica). *Veterinary Microbiology*. 2017-05 2017;203:95-102. doi:10.1016/j.vetmic.2017.03.003

159. Gao R, Cao B, Hu Y, Feng Z, Wang D, Hu W. Human Infection with a Novel Avian-Origin Influenza A (H7N9) Virus. research-article. Updated 2013-05-15. https://www.nejm.org/doi/10.1056/NEJMoa1304459

160. Kageyama T, Fujisaki S, Takashita E, et al. Rapid communication Genetic analysis of novel avian A(H7N9) influenza viruses isolated from patients in China, February to April 2013. *Euro Surveillance Bulletin*. 2013-4-11 2013;18(15):20453.

161. USDA. Epidemiologic and Other Analyses of HPAI/LPAI Affected Poultry Flocks. Updated 3/2016. https://www.aphis.usda.gov/animal_health/downloads/animal_diseases/ai/epi-analyses-avian-flu-poultry.pdf

162. WHO. Avian Influenza Weekly Update Number 828. Updated 1/21/2022. https://www.who.int/westernpacific/emergencies/surveillance/avian-influenza

163. Ostrowsky B, Huang A, Terry W, et al. Low Pathogenic Avian Influenza A (H7N2) Virus Infection in Immunocompromised Adult, New York, USA, 2003. *Emerging Infectious Diseases*. July 2012 2012;18(7):1128. doi:10.3201/eid1807.111913

164. Eurosurveillance. Avian influenza A/(H7N2) outbreak in the United Kingdom. *Weekly releases (1997–2007)*. 2007/05/31 2007;12(22):3206. doi:10.2807/esw.12.22.03206-en

165. Belser JA, Creager HM, Zeng H, Maines TR, Tumpey TM. Pathogenesis, Transmissibility, and Tropism of a Highly Pathogenic Avian Influenza A(H7N7) Virus Associated With Human Conjunctivitis in Italy, 2013. *The Journal of infectious diseases*. 2017-9-15 2017;216(Suppl 4):S508-S511. doi:10.1093/infdis/jiw559

166. Tweed SA, Skowronski DM, David ST, et al. Human Illness from Avian Influenza H7N3, British Columbia. *Emerging Infectious Diseases*. December 2004 2004;10(12):2196. doi:10.3201/eid1012.040961

167. Wei S-H, Yang J-R, Wu H-S, et al. Human infection with avian influenza A H6N1 virus: an epidemiological analysis. *The Lancet Respiratory Medicine*. 2013-12 2013;1(10):771-778. doi:10.1016/S2213-2600(13)70221-2

168. Peacock ThP, James J, Sealy JE, Iqbal M. A Global Perspective on H9N2 Avian Influenza Virus. *Viruses*. 2019-7-05 2019;11(7):620. doi:10.3390/v11070620

169. Kandeel A, Manoncourt S, Kareem EAe, et al. Zoonotic Transmission of Avian Influenza Virus (H5N1), Egypt, 2006–2009. *Emerging Infectious Diseases journal*. July 2010 2010;16(7) doi:10.3201/eid1607.091695

170. Peng L, Chen C, Kai-yi H, et al. Molecular characterization of H9N2 influenza virus isolated from mink and its pathogenesis in mink. *Veterinary Microbiology*. 2015-03-23 2015;176(1-2):88-96. doi:10.1016/j.vetmic.2015.01.009

171. Song D, Kang B, Lee C, et al. Transmission of Avian Influenza Virus (H3N2) to Dogs. *Emerging Infectious Diseases*. 2008-5 2008;14(5):741-746. doi:10.3201/eid1405.071471

172. Wang J, Wu M, Hong W, et al. Infectivity and Transmissibility of Avian H9N2 Influenza Viruses in Pigs. *Journal of Virology*. 2016-01-13 2016;90(7):3506-3514. doi:10.1128/JVI.02605-15

173. Yan Y, Gu J-Y, Yuan Z-C, et al. Genetic characterization of H9N2 avian influenza virus in plateau pikas in the Qinghai Lake region of China. *Archives of Virology*. 2017-04 2017;162(4):1025-1029. doi:10.1007/s00705-016-3176-1

174. Guo Y, Li J, Cheng X. Discovery of men infected by avian influenza A (H9N2) virus. *Chinese Journal of Experimental and Clinical Virology*. 1999-06-30 1999;13(2):105-108.

175. Peiris M, Yuen KY, Leung CW, et al. Human infection with influenza H9N2. *Lancet (London, England)*. 1999-09-11 1999;354(9182):916-917. doi:10.1016/s0140-6736(99)03311-5

176. Organization PAH. Avian Influenza Virus A (H10N7) Circulating among Humans in Egypt - Vol. 2, No. 18—7 May 2004 - PAHO/WHO | Pan American Health Organization. Updated 2004. https://www.paho.org/en/documents/avian-influenza-virus-h10n7-circulating-among-humans-egypt-vol-2-no-18-7-may-2004

177. Arzey GG, Kirkland PD, Arzey KE, et al. Influenza Virus A (H10N7) in Chickens and Poultry Abattoir Workers, Australia - Volume 18, Number 5—May 2012. *Emerging Infectious Diseases*. 5/2012 2012;doi:10.3201/eid1805.111852

178. Krog JS, Hansen MS, Holm E, et al. Influenza A(H10N7) Virus in Dead Harbor Seals, Denmark - Volume 21, Number 4—April 2015 - Emerging Infectious Diseases journal - CDC. *Emerging Infectious Diseases*. 2015 2015;doi:10.3201/eid2104.141484

179. Zhang T, Bi Y, Tian H, et al. Human Infection with Influenza Virus A(H10N8) from Live Poultry Markets, China, 2014. *Emerging Infectious Diseases*. 12/2014 2014;doi:10.3201/eid2012.140911

180. Cui L, Liu D, Shi W, et al. Dynamic reassortments and genetic heterogeneity of the human-infecting influenza A (H7N9) virus. *Nature Communications*. 2014 2014;5:3142. doi:10.1038/ncomms4142

181. CDC. Highly Pathogenic Asian Avian Influenza A(H5N1) in People | Avian Influenza (Flu). Updated 2018-12-11T10:51:43Z/. https://www.cdc.gov/flu/avianflu/spotlights/2022-2023/h5n1-technical-report_september.htm

182. Ellis TM, Bousfield RB, Bissett LA, et al. Investigation of outbreaks of highly pathogenic H5N1 avian influenza in waterfowl and wild birds in Hong Kong in late 2002. *Avian Pathology: Journal of the WVPA*. 2004-10 2004;33(5):492-505. doi:10.1080/03079450400003601

183. Jimenez-Bluhm P, Sepulveda A, Baumberger C, et al. Evidence of influenza infection in dogs and cats in central Chile. *Preventive Veterinary Medicine*. 2021-04-16 2021;191:105349. doi:10.1016/j.prevetmed.2021.105349

184. Guan Y, Peiris JSM, Lipatov AS, et al. Emergence of multiple genotypes of H5N1 avian influenza viruses in Hong Kong SAR. *Proceedings of the National Academy of Sciences of the United States of America*. 25 June 2002 2002;99(13):8950. doi:10.1073/pnas.132268999

185. Sims LD, Ellis TM, Liu KK, et al. Avian influenza in Hong Kong 1997-2002. *Avian Diseases*. 2003 2003;47(3 Suppl):832-838. doi:10.1637/0005-2086-47.s3.832

186. Sims LD, Domenech J, Benigno C, et al. Origin and evolution of highly pathogenic H5N1 avian influenza in Asia. *The Veterinary Record*. 2005-08-06 2005;157(6):159-164. doi:10.1136/vr.157.6.159

187. Chen H, Smth G, Zhang S. H5N1 virus outbreak in migratory waterfowl. Updated 2005. https://www.nature.com/articles/nature03974

188. Sonnberg S, Webby RJ, Webster RG. 2.1 Natural History of Highly Pathogenic Avian Influenza H5N1. *Virus research*. 2013-12-5 2013;178(1):10.1016/j.virusres.2013.05.009. doi:10.1016/j.virusres.2013.05.009

189. WHO. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2021. Updated 12/13/2021. https://cdn.who.int/media/docs/default-source/influenza/h5n1-human-case-cumulative-table/2021_april_tableh5n1.pdf?sfvrsn=fc40672c_5&download=true

190. WHO. *Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2017*. 2017. 2017. https://www.who.int/publications/m/item/cumulative-number-of-confirmed-human-cases-for-avian-influenza-a(h5n1)-reported-to-who--2003-2023-1-november-2023

191. WHO. Influenza at the human-animal interface Summary and assessment, from 14 December 2021 to 21 January 2022. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_jan_2022.pdf?sfvrsn=1893dd9f_5&download=true

192. ProMED. Home - ProMED. https://promedmail.org/

193. Mathur MB, Patel RB, Gould M, et al. Seasonal Patterns in Human A (H5N1) Virus Infection: Analysis of Global Cases. *PLoS ONE*. 2014-9-12 2014;9(9):e106171. doi:10.1371/journal.pone.0106171

194. Ip HS, Torchetti MK, Crespo R, et al. Novel Eurasian Highly Pathogenic Avian Influenza A H5 Viruses in Wild Birds, Washington, USA, 2014 - Volume 21, Number 5—May 2015 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. 5/2015 2015;doi:10.3201/eid2105.142020

195. Bevins S, Dusek R, White C, Gidlewski T. Large-Scale Avian Influenza Surveillance in Wild Birds throughout the United States. *PLoS Medicine*. 8/14/2014 2014;doi: https://doi.org/10.1371%2Fjournal.pone.0104360

196. USDA. USDA APHIS | 2014-2015 HPAI Outbreak. Updated 2015.

197. Patel MC, Chesnokov A, Jones J, et al. Susceptibility of widely diverse influenza a viruses to PB2 polymerase inhibitor pimodivir. *Antiviral Research*. 04/2021 2021;188:105035. doi:10.1016/j.antiviral.2021.105035

198. Jiang H, Wu P, Uyeki TM, et al. Preliminary Epidemiologic Assessment of Human Infections With Highly Pathogenic Avian Influenza A(H5N6) Virus, China. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*. 2017-8-01 2017;65(3):383-388. doi:10.1093/cid/cix334

199. Mok CKP, Guan WD, Liu XQ, et al. Genetic Characterization of Highly Pathogenic Avian Influenza A(H5N6) Virus, Guangdong, China. *Emerging Infectious Diseases journal*. December 2015 2015;21(12)doi:10.3201/eid2112.150809

200. Lee K, Lee E-K, Lee H, et al. Highly Pathogenic Avian Influenza A(H5N6) in Domestic Cats, South Korea. *Emerging Infectious Diseases*. 12/2018 2018;24(12):2343-2347. doi:10.3201/eid2412.180290

201. Li Y, Li M, Li Y, et al. Outbreaks of Highly Pathogenic Avian Influenza (H5N6) Virus Subclade 2.3.4.4h in Swans, Xinjiang, Western China, 2020. *Emerging Infectious Diseases journal*. December 2020 2020;26(12)doi:10.3201/eid2612.201201

202. CDC. CDC Update on A(H5N6) Bird Flu. Updated 2021-11-01. https://www.cdc.gov/flu/avianflu/index.htm

203. CIDRAP. Russia reports first human H5N8 avian flu cases. Updated 2021. https://www.cidrap.umn.edu/russia-reports-first-human-h5n8-avian-flu-cases

204. Tajudeen YA. Emerging Strain (H5N8) of Highly Pathogenic Avian Influenza Virus: An Impending Pandemic Threat. *Journal of Infectious Diseases and Epidemiology*. 2021/07/19 2021;7(7):217. doi:10.23937/2474-3658/1510217

205. Harder T, Maurer-Stroh S, Pohlmann A, et al. Influenza A(H5N8) Virus Similar to Strain in Korea Causing Highly Pathogenic Avian Influenza in Germany. *Emerging Infectious Diseases journal*. May 2015 2015;21(5)doi:10.3201/eid2105.141897

206. Bouwstra R, Heutink R, Bossers A, Harders F, Koch G, Elbers A. Full-Genome Sequence of Influenza A(H5N8) Virus in Poultry Linked to Sequences of Strains from Asia, the Netherlands, 2014. *Emerging Infectious Diseases*. 2015-05 2015;21(5):872-874. doi:10.3201/eid2105.141839

207. Lee D-H, Torchetti MK, Winker K, Ip HS, Song C-S, Swayne DE. Intercontinental Spread of Asian-Origin H5N8 to North America through Beringia by Migratory Birds. *Journal of Virology*. 2015-4-8 2015;89(12):6521-6524. doi:10.1128/JVI.00728-15

208. Napp S, Majó N, Sánchez-Gónzalez R, Vergara-Alert J. Emergence and spread of highly pathogenic avian influenza A(H5N8) in Europe in 2016-2017. *Transboundary and Emerging Diseases*. 2018-10 2018;65(5):1217-1226. doi:10.1111/tbed.12861

209. Lewis NS, Banyard AC, Whittard E, et al. Emergence and spread of novel H5N8, H5N5 and H5N1 clade 2.3.4.4 highly pathogenic avian influenza in 2020. *Emerging Microbes & Infections*. 2021-12 2021;10(1):148-151. doi:10.1080/22221751.2021.1872355

210. Baek Y-G, Lee Y-N, Lee D-H, et al. Multiple Reassortants of H5N8 Clade 2.3.4.4b Highly Pathogenic Avian Influenza Viruses Detected in South Korea during the Winter of 2020-2021. *Viruses*. 2021-03-16 2021;13(3):490. doi:10.3390/v13030490

211. Isoda N, Twabela AT, Bazarragchaa E, et al. Re-Invasion of H5N8 High Pathogenicity Avian Influenza Virus Clade 2.3.4.4b in Hokkaido, Japan, 2020. *Viruses*. 2020-12-14 2020;12(12):E1439. doi:10.3390/v12121439

212. Jeoung H-Y, Lim S-I, Shin B-H, et al. A novel canine influenza H3N2 virus isolated from cats in an animal shelter. *Veterinary Microbiology*. 2013-08-30 2013;165(3-4):281-286. doi:10.1016/j.vetmic.2013.03.021

213. Li X, Lv X, Li Y, et al. Highly Pathogenic Avian Influenza A(H5N8) Virus in Swans, China, 2020 - Volume 27, Number 6—June 2021 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. 6/2021 2021;doi:10.3201/eid2706.204727

214. Molini U, Aikukutu G, Roux J-P, et al. Avian Influenza H5N8 Outbreak in African Penguins (Spheniscus demersus), Namibia, 2019. *Journal of Wildlife Diseases*. 2020-01 2020;56(1):214-218.

215. Shin D-L, Siebert U, Lakemeyer J, et al. Highly Pathogenic Avian Influenza A(H5N8) Virus in Gray Seals, Baltic Sea. *Emerging Infectious Diseases*. 2019-12 2019;25(12):2295-2298. doi:10.3201/eid2512.181472

216. Floyd T, Banyard AC, Lean FZX, Byrne AMP, Fullick E, Whittard E. Encephalitis and Death in Wild Mammals at a Rehabilitation Center after Infection with Highly Pathogenic Avian Influenza A(H5N8) Virus, United Kingdom - Volume 27, Number 11—November 2021 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. 2021;doi:10.3201/eid2711.211225

217. WHO. Avian influenza A(H5N8) infects humans in Russian Federation. Updated 2021. https://www.who.int/emergencies/disease-outbreak-news/item/2021-DON313

218. CDC. Notes from the Field: Highly Pathogenic Avian Influenza A (H7N3) Virus Infection in Two Poultry Workers — Jalisco, Mexico, July 2012. *MMWR Morb Mortal Wkly Rep*. 9/14/2012 2012;61

219. Vijaykrishna D, Deng Y-M, Grau ML, et al. Emergence of Influenza A(H7N4) Virus, Cambodia - Volume 25, Number 10. *Emerging Infectious Diseases*. 10/2019 2019;doi:10.3201/eid2510.190506

220. Chai H, Li X, Li M, Lv X, Yu W, Li Y. Emergence, Evolution, and Pathogenicity of Influenza A(H7N4) Virus in Shorebirds, China. *Journal of Virology*. 2021-11-17 2021:JVI0171721. doi:10.1128/JVI.01717-21

221. Tong X-C, Weng S-S, Xue F, Wu X, Xu T-M, Zhang W-H. First human infection by a novel avian influenza A(H7N4) virus. *The Journal of Infection*. 2018-09 2018;77(3):249-257. doi:10.1016/j.jinf.2018.06.002

222. Taylor HR, Turner AJ. A case report of fowl plague keratoconjunctivitis. *The British Journal of Ophthalmology*. 1977-02 1977;61(2):86-88. doi:10.1136/bjo.61.2.86

223. Geraci JR, St. Aubin DJ, Barker IK, Webster RG, Hinshaw VS. Mass Mortality of Harbor Seals: Pneumonia Associated with Influenza A Virus. *Science*. 1982 1982;215(4536):1129-1131. doi: https://doi.org/10.1126/science.7063847

224. Koopmans M, Wilbrink B, Conyn M, et al. Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands. *The Lancet*. 2004-02-21 2004;363(9409):587-593. doi:10.1016/S0140-6736(04)15589-X

225. Puzelli S, Rizzo C, Fabiani C, et al. Influenza A(H7N7) Virus among Poultry Workers, Italy, 2013. *Emerging Infectious Diseases*. 2016-8 2016;22(8):1512-1513. doi:10.3201/eid2208.160246

226. USDA. Epidemiologic and Other Analyses of Indiana HPAI/LPAI-Affected Poultry Flocks. Updated 2016. https://www.aphis.usda.gov/animal_health/downloads/animal_diseases/ai/epi-analyses-avian-flu-poultry.pdf

227. USDA. USDA APHIS | 2016 HPAI/LPAI Findings in Indiana. Updated 2016. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/emergency-management/hpai/fadprep-hpai

228. Brown JA. Public Health Response to an Avian Influenza A(H7N8) Virus Outbreak in Commercial Turkey Flocks — Indiana, 2016. *MMWR Morbidity and Mortality Weekly Report*. 2018 2018;67doi:10.15585/mmwr.mm6748a2

229. Pan Y, Cui S, Sun Y, et al. Human infection with H9N2 avian influenza in northern China. *Clinical Microbiology and Infection: The Official Publication of the European Society of Clinical Microbiology and Infectious Diseases*. 2018-03 2018;24(3):321-323. doi:10.1016/j.cmi.2017.10.026

230. Floyd T, Banyard AC, Lean FZX, Byrne AMP, Fullick E, Whittard E. Encephalitis and Death in Wild Mammals at a Rehabilitation Center after Infection with Highly Pathogenic Avian Influenza A(H5N8) Virus, United Kingdom. *Emerging infectious diseases*. 2021 Nov 2021;27(11) doi:10.3201/eid2711.211225

231. Cao X, Yang F, Wu H, Xu L. Genetic characterization of novel reassortant H5N6-subtype influenza viruses isolated from cats in eastern China. *Archives of Virology*. 2017-11 2017;162(11):3501-3505. doi:10.1007/s00705-017-3490-2

232. WHO. Human infection with avian influenza A(H5) viruses - April 2022. https://www.who.int/docs/default-source/wpro---documents/emergency/surveillance/avian-influenza/ai-20220401.pdf?sfvrsn=30d65594_220

233. WHO. Human infection with avian influenza A(H10N3) – China. Updated 2021. https://www.who.int/emergencies/disease-outbreak-news/item/human-infection-with-avian-influenza-a(h10n3)-china

234. Chen S, Li Z, Hu M, et al. Knowledge, Attitudes, and Practices (KAP) Relating to Avian Influenza (H10N8) among Farmers' Markets Workers in Nanchang, China. *PLoS ONE*. 2015-5-18 2015;10(5):e0127120. doi:10.1371/journal.pone.0127120

235. CDC. Current Bird Flu Situation in Poultry | Avian Influenza (Flu). Updated 2022-06-14T04:27:48Z. https://www.cdc.gov/flu/avianflu/poultry.htm

236. Chen W, Zhang X, Zhao W. Environmental factors and spatiotemporal distribution characteristics of the global outbreaks of the highly pathogenic avian influenza H5N1. *Environmental science and pollution research international*. 2022 Jun 2022;29(29)doi:10.1007/s11356-022-19016-1

237. Prevention and Control of H5 and H7 Avian Influenza in the Live Bird Marketing System (USDA) 26 (2016).

238. WOAH. WOAH-WAHIS. https://www.woah.org/en/home/

239. Grillo V, Arzey K, Hansbro P, et al. Avian influenza in Australia: a summary of 5 years of wild bird surveillance. *Australian Veterinary Journal*. 2015 2015;93(11):387-393. doi:10.1111/avj.12379

240. Jiménez-Bluhm P, Karlsson EA, Freiden P, et al. Wild birds in Chile Harbor diverse avian influenza A viruses. *Emerging Microbes & Infections*. 2018-12-01 2018;7(1):1-4. doi:10.1038/s41426-018-0046-9

241. USDA. *Epidemiologic analyses of avian influenza in poultry*. 2020. 2020. Accessed 2021-10-09 22:19:29. https://www.aphis.usda.gov/animal_health/downloads/animal_diseases/ai/epi-analyses-avian-flu-poultry.pdf

242. USDA. USDA APHIS | What is Influenza A Virus in Swine (IAV-S). Updated 2021.

243. Nardelli L, Pascucci S, Gualandi GL, Loda P. Outbreaks of classical swine influenza in Italy in 1976. *Zentralblatt Fur Veterinarmedizin Reihe B Journal of Veterinary Medicine Series B*. 1978-12 1978;25(10):853-857. doi:10.1111/j.1439-0450.1978.tb01062.x

244. Campitelli L, Donatelli I, Foni E, et al. Continued evolution of H1N1 and H3N2 influenza viruses in pigs in Italy. *Virology*. 1997-06-09 1997;232(2):310-318. doi:10.1006/viro.1997.8514

245. Detmer S, Gramer M, Goyal S, Torremorell M, Torrison J. Diagnostics and Surveillance for Swine Influenza. *Swine Influenza*. 2012-5-8 2012;370:85-112. doi:10.1007/82_2012_220

246. Kluska V, Macku M, Mensik J. Demonstration of antibodies against swine influenza viruses in man. *Ceskoslovenska Pediatrie*. 1961-05 1961;16:408-414.

247. Smith TF, Burgert EO, Dowdle WR, Noble GR, Campbell RJ, Van Scoy RE. Isolation of Swine Influenza Virus from Autopsy Lung Tissue of Man. *New England Journal of Medicine*. March 25, 1976 1976;294(13):708-710. doi:10.1056/NEJM197603252941308

248. Shinde V, Bridges CB, Uyeki TM, et al. Triple-Reassortant Swine Influenza A (H1) in Humans in the United States, 2005–2009. *New England Journal of Medicine*. June 18, 2009 2009;360(25):2616-2625. doi:10.1056/NEJMoa0903812

249. Health Na. Avian Influenza History. Updated 2014-11-27. https://nurseandhealth.wordpress.com/2014/11/27/86/

250. Statistica. Pig population worldwide. Updated 3/2018. https://www.statista.com/statistics/263963/number-of-pigs-worldwide-since-1990/#:~:text=They%20are%20the%20primary%20protein%20source%20for%20millions,around%20750%20million%20heads%20in%20the%20previous%20year.

251. Thontiravong A, Kitikoon P, Wannaratana S, et al. Quail as a potential mixing vessel for the generation of new reassortant influenza A viruses. *Veterinary Microbiology*. 2012-12-07 2012;160(3-4):305-313. doi:10.1016/j.vetmic.2012.05.043

252. Smith GJD, Vijaykrishna D, Bahl J, et al. Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic. *Nature*. 2009-06 2009;459(7250):1122-1125. doi:10.1038/nature08182

253. Karasin AI, Brown IH, Carman S, Olsen CW. Isolation and Characterization of H4N6 Avian Influenza Viruses from Pigs with Pneumonia in Canada. *Journal of Virology*. October 1, 2000 2000;74(19):9322-9327. doi:10.1128/JVI.74.19.9322-9327.2000

254. Vincent AL, Swenson SL, Lager KM, Gauger PC, Loiacono C, Zhang Y. Characterization of an influenza A virus isolated from pigs during an outbreak of respiratory disease in swine and people during a county fair in the United States. *Veterinary Microbiology*. 2009-05-28 2009;137(1-2):51-59. doi:10.1016/j.vetmic.2009.01.003

255. Anderson TK, Nelson MI, Kitikoon P, Swenson SL, Korslund JA, Vincent AL. Population dynamics of cocirculating swine influenza A viruses in the United States from 2009 to 2012. *Influenza and Other Respiratory Viruses*. 2013-12 2013;7 Suppl 4:42-51. doi:10.1111/irv.12193

256. Bravo-Vasquez N, Karlsson EA, Jimenez-Bluhm P, et al. Swine Influenza Virus (H1N2) Characterization and Transmission in Ferrets, Chile. *Emerging Infectious Diseases*. 2/2017 2017;doi:10.3201/eid2302.161374

257. Kubota-Koketsu R, Yunoki M, Okuno Y, Ikuta K. Significant neutralizing activities against H2N2 influenza A viruses in human intravenous immunoglobulin lots manufactured from 1993 to 2010. *Biologics : Targets & Therapy*. 2012 2012;6:245-247. doi:10.2147/BTT.S33495

258. CDC. Current U.S. Bird Flu Situation in Humans. https://www.cdc.gov/flu/avianflu/inhumans.htm

259. Beaudoin A, Johnson S, Davies P, Bender J, Gramer M. Characterization of Influenza A Outbreaks in Minnesota Swine Herds and Measures Taken to Reduce the Risk of Zoonotic Transmission. *Zoonoses and Public Health*. 2012 2012;59(2):96-106. doi:10.1111/j.1863-2378.2011.01423.x

260. Bowman AS, Nolting JM, Nelson SW, Slemons RD. Subclinical Influenza Virus A Infections in Pigs Exhibited at Agricultural Fairs, Ohio, USA, 2009–2011. *Emerging Infectious Diseases journal*. December 2012 2012;18(12)doi:10.3201/eid1812.121116

261. CDC. H3N2v and You | CDC. Updated 2020-01-29T09:06:44Z. https://www.cdc.gov/flu/swineflu/variant-flu-in-humans.htm

262. Cox CM, Neises D, Garten RJ, et al. Swine Influenza Virus A (H3N2) Infection in Human, Kansas, USA, 2009. *Emerging Infectious Diseases*. June 2011 2011;17(6):1143. doi:10.3201/eid1706.101488

263. Deng Y-M, Wong FYK, Spirason N, et al. Locally Acquired Human Infection with Swine-Origin Influenza A(H3N2) Variant Virus, Australia, 2018. *Emerging Infectious Diseases journal*. January 2020 2020;26(1)doi:10.3201/eid2601.191144

264. Zhang G, Kong W, Qi W, et al. Identification of an H6N6 swine influenza virus in southern China. *Infection, Genetics and Evolution: Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases*. 2011-07 2011;11(5):1174-1177. doi:10.1016/j.meegid.2011.02.023

265. Morens DM, Taubenberger JK. Historical thoughts on influenza viral ecosystems, or behold a pale horse, dead dogs, failing fowl, and sick swine. *Influenza and Other Respiratory Viruses*. 2010 2010;4(6):327-337. doi:10.1111/j.1750-2659.2010.00148.x

266. Sack A, Cullinane A, Daramragchaa U, Chuluunbaatar M, Gonchigoo B, Gray GC. Equine Influenza Virus—A Neglected, Reemergent Disease Threat. *Emerging Infectious Diseases*. 06/2019 2019;25(6):1185-1191. doi:10.3201/eid2506.161846

267. Yondon M, Heil GL, Burks JP, et al. Isolation and characterization of H3N8 equine influenza A virus associated with the 2011 epizootic in Mongolia. *Influenza and Other Respiratory Viruses*. 2013-09 2013;7(5):659-665. doi:10.1111/irv.12069

268. Perglione CO, Gildea S, Rimondi A, et al. Epidemiological and virological findings during multiple outbreaks of equine influenza in South America in 2012. *Influenza and Other Respiratory Viruses*. 2016-1 2016;10(1):37-46. doi:10.1111/irv.12349

269. Qi T, Guo W, Huang W, et al. Isolation and genetic characterization of H3N8 equine influenza virus from donkeys in China. *Veterinary Microbiology*. 2010-08-26 2010;144(3-4):455-460. doi:10.1016/j.vetmic.2010.01.006

270. Su S, Wang L, Fu X, et al. Equine Influenza A(H3N8) Virus Infection in Cats. *Emerging Infectious Diseases*. 12/2014 2014;doi:10.3201/eid2012.140867

271. Sack A, Oladunni FS, Gonchigoo B, Chambers TM, Gray GC. Zoonotic Diseases from Horses: A Systematic Review. *Vector-Borne and Zoonotic Diseases*. 2020-07-01 2020;20(7):484-495. doi:10.1089/vbz.2019.2541

272. Xie T, Anderson BD, Daramragchaa U, Chuluunbaatar M, Gray GC. A Review of Evidence that Equine Influenza Viruses Are Zoonotic. *Pathogens*. 2016-7-12 2016;5(3):50. doi:10.3390/pathogens5030050

273. Luis Dionisio FM, Manuel Pequito, Ana Faustino-Rocha. Equine influenza: a comprehensive review from etiology to treatment. *Animal Health Research Reviews*. 2021;22(1)

274. Bryant NA, Rash AS, Russell CA, et al. Antigenic and genetic variations in European and North American equine influenza virus strains (H3N8) isolated from 2006 to 2007. *Veterinary Microbiology*. 2009-07-02 2009;138(1-2):41-52. doi:10.1016/j.vetmic.2009.03.004

275. Bryant NA, Rash AS, Woodward AL, et al. Isolation and characterisation of equine influenza viruses (H3N8) from Europe and North America from 2008 to 2009. *Veterinary Microbiology*. 2011-01-10 2011;147(1-2):19-27. doi:10.1016/j.vetmic.2010.05.040

276. Daly JM. Equine influenza: A review of an unpredictable virus. *The Veterinary Journal*. 2011 2011:8. doi:https://doi.org/10.1016/j.tvjl.2010.06.026

277. Madić J, Martinović S, Naglić T, Hajsig D, Cvetnić S. Serological evidence for the presence of A/equine-I influenza virus in unvaccinated horses in Croatia. *The Veterinary record*. February 1, 1996 1996;138:68. doi:10.1136/vr.138.3.68

278. Sovinova O, Tumova B, Pouska F, Nemec J. Isolation of a virus causing respiratory disease in horses. *Acta Virologica*. 1958 Jan-Mar 1958;2(1):52-61.

279. WOAH. WOAH Expert Surveillance Panel on Equine Influenza Vaccine Composition. *WOAH Bulletin* blog. 2020. Accessed 2021-11-15 00:00:31. https://www.woah.org/app/uploads/2022/10/expert-surveillance-panel-on-equine-influenza-vaccine-composition.pdf

280. Management BoL. A virus has been identified as the principal cause of the outbreak and mortality at BLM's wild horse and burro facility | Bureau of Land Management. https://www.blm.gov/press-release/virus-has-been-identified-principal-cause-outbreak-and-mortality-blms-wild-horse-and

281. Borland S, Gracieux P, Jones M, Mallet F, Yugueros-Marcos J. Influenza A Virus Infection in Cats and Dogs: A Literature Review in the Light of the "One Health" Concept. *Frontiers in Public Health*. 2020-3-20 2020;8:83. doi:10.3389/fpubh.2020.00083

282. Lyoo K-S, Kim J-K, Kang B, et al. Comparative analysis of virulence of a novel, avian-origin H3N2 canine influenza virus in various host species. *Virus research*. 2015-01-01 2015;195:135-140. doi:10.1016/j.virusres.2014.08.020

283. Wasik BR, Voorhees IEH, Parrish CR. Canine and Feline Influenza. *Cold Spring Harbor Perspectives in Medicine*. 01/2021 2021;11(1):a038562. doi:10.1101/cshperspect.a038562

284. Chen Y, Trovão NS, Wang G, et al. Emergence and Evolution of Novel Reassortant Influenza A Viruses in Canines in Southern China. *mBio*. 2018-6-5 2018;9(3):e00909-18. doi:10.1128/mBio.00909-18

285. Ramírez-Martínez LA, Contreras-Luna M, De la Luz J, et al. Evidence of transmission and risk factors for influenza A virus in household dogs and their owners. *Influenza and Other Respiratory Viruses*. 2013-11 2013;7(6):1292-1296. doi:10.1111/irv.12162

286. Song D, Kim H, Na W, et al. Canine susceptibility to human influenza viruses (A/pdm 09H1N1, A/H3N2 and B). *Journal of General Virology*. 2015 2015;96(2):254-258. doi:10.1099/vir.0.070821-0

287. Crawford PC, Dubovi EJ, Castleman WL, et al. Transmission of Equine Influenza Virus to Dogs. *Science*. 2005-10-21 2005;310(5747):482-485. doi:10.1126/science.1117950

288. Hayward JJ, Dubovi EJ, Scarlett JM, Janeczko S, Holmes EC, Parrish CR. Microevolution of Canine Influenza Virus in Shelters and Its Molecular Epidemiology in the United States. *Journal of Virology*. December 2010 2010;84(24):12636. doi:10.1128/JVI.01350-10

289. University C. Cornell University Baker Institute. 2022.

290. University IS. Canine Influenza. https://vetmed.iastate.edu/vdpam/research/disease-topics/influenza/canine-influenza

291. NBC. Canine Influenza Outbreak Dissipates at LA City Animal Shelters. *NBC Los Angeles* blog. 2021. Accessed 2021-12-18 21:25:46. https://mynewsla.com/orange-county/2021/12/09/canine-influenza-outbreak-dissipates-at-la-city-animal-shelters/

292. CDC. Canine Influenza. Updated 2018-09-27T12:56:01Z/. https://www.cdc.gov/flu/other/canine-flu/keyfacts.html

293. Health MBoA. New guidance for pet owners to combat community spread of canine influenza virus | Minnesota Board of Animal Health. https://www.bah.state.mn.us/news_release/new-guidance-for-pet-owners-to-combat-community-spread-of-canine-influenza-virus/

294. Times NY. Dog Flu Is Back, Too. @nytimes. Updated 2022-12-02. https://www.nytimes.com/2022/12/02/health/dogs-canine-flu.html

295. News C. Dog flu cases on the rise in some U.S. regions this winter season. @CBSNews. https://www.cbsnews.com/news/dog-flu-canine-influenza-rise-winter/

296. ABC11_WTVD. NC veterinarians warn of outbreak in dog flu cases in Durham, Moore counties. @ABC11_WTVD. Updated 2023-04-21. https://abc11.com/pets-dog-flu-outbreak-canine-influenza-symptoms/13164509/

297. Daly JM, Blunden AS, MacRae S, et al. Transmission of Equine Influenza Virus to English Foxhounds. *Emerging Infectious Diseases*. 2008-3 2008;14(3):461-464. doi:10.3201/eid1403.070643

298. Kirkland PD, Finlaison DS, Crispe E, Hurt AC. Influenza Virus Transmission from Horses to Dogs, Australia. *Emerging Infectious Diseases*. 2010-4 2010;16(4):699-702. doi:10.3201/eid1604.091489

299. Krueger WS, Heil GL, Yoon K-J, Gray GC. No evidence for zoonotic transmission of H3N8 canine influenza virus among US adults occupationally exposed to dogs. *Influenza and Other Respiratory Viruses*. 2014-1 2014;8(1):99-106. doi:10.1111/irv.12208

300. Voorhees IEH, Glaser AL, Toohey-Kurth KL, et al. Spread of Canine Influenza A(H3N2) Virus, United States. *Emerging Infectious Diseases*. 12/2017 2017;doi:10.3201/eid2312.170246

301. Gutman SN, Guptill LF, Moore GE, Pogranichniy RM. Serologic investigation of exposure to influenza A virus H3N2 infection in dogs and cats in the United States. *Journal of Veterinary Diagnostic Investigation*. 03/2019 2019;31(2):250-254. doi:10.1177/1040638718824357

302. Zhu H, Hughes J, Murcia PR. Origins and Evolutionary Dynamics of H3N2 Canine Influenza Virus. *Journal of Virology*. 2015-3-4 2015;89(10):5406-5418. doi:10.1128/JVI.03395-14

303. Department LCH. Animal Health Alert: Update on Influenza and Leptospirosis in Dogs. Updated 2021. http://www.publichealth.lacounty.gov/vet/docs/AHAN/AHAN_UpdateInfluenzaLeptoDogs_08132021.pdf

304. Campagnolo ER, Rankin JT, Daverio SA, et al. Fatal pandemic (H1N1) 2009 influenza A virus infection in a Pennsylvania domestic cat. *Zoonoses and public health*. 2011-11-01 2011;58(7):500-507. doi:10.1111/j.1863-2378.2011.01390.x

305. Song DS, An DJ, Moon HJ, et al. Interspecies transmission of the canine influenza H3N2 virus to domestic cats in South Korea, 2010. *Journal of General Virology*. 2010 2010;92(10):2350-2355. doi:10.1099/vir.0.033522-0

306. Keawcharoen J, Oraveerakul K, Kuiken T, et al. Avian Influenza H5N1 in Tigers and Leopards - Volume 10, Number 12—December 2004. *MMWR Morb Mortal Wkly Rep*. 12/2004 2004;doi:10.3201/eid1012.040759

307. Thanawongnuwech R, Amonsin A, Tantilertcharoen R, et al. Probable Tiger-to-Tiger Transmission of Avian Influenza H5N1. *Emerging Infectious Diseases*. 2005-5 2005;11(5):699-701. doi:10.3201/eid1105.050007

308. Marschall J, Schulz B, Priv-Doz TCH, et al. Prevalence of influenza A H5N1 virus in cats from areas with occurrence of highly pathogenic avian influenza in birds. *Journal of Feline Medicine and Surgery*. August 1, 2008 2008;10(4):355-358. doi:10.1016/j.jfms.2008.03.007

309. Belser JA, Pulit-Penaloza JA, Sun X, et al. A Novel A(H7N2) Influenza Virus Isolated from a Veterinarian Caring for Cats in a New York City Animal Shelter Causes Mild Disease and Transmits Poorly in the Ferret Model. *Journal of Virology*. 2017-08-01 2017;91(15):e00672-17. doi:10.1128/JVI.00672-17

310. Hatta M, Zhong G, Gao Y, et al. Characterization of a Feline Influenza A(H7N2) Virus. *Emerging Infectious Diseases*. 1/2018 2018;doi:10.3201/eid2401.171240

311. Tong S, Li Y, Rivailler P, et al. A distinct lineage of influenza A virus from bats. *Proceedings of the National Academy of Sciences*. 2012/03/13 2012;109(11):4269-4274. doi:10.1073/pnas.1116200109

312. Tong S, Zhu X, Li Y, et al. New World Bats Harbor Diverse Influenza A Viruses. *PLOS Pathogens*. Oct 10, 2013 2013;9(10):e1003657. doi:10.1371/journal.ppat.1003657

313. Ciminski K, Schwemmle M. Bat-Borne Influenza A Viruses: An Awakening. *Cold Spring Harbor Perspectives in Medicine*. 02/2021 2021;11(2):a038612. doi:10.1101/cshperspect.a038612

314. Campos ACA, Góes LGB, Moreira-Soto A, et al. Bat Influenza A(HL18NL11) Virus in Fruit Bats, Brazil. *Emerging Infectious Diseases*. 2/2019 2019;doi:10.3201/eid2502.181246

315. Freidl GS, Binger T, Müller MA, et al. Serological Evidence of Influenza A Viruses in Frugivorous Bats from Africa. *PLOS ONE*. May 12, 2015 2015;10(5):e0127035. doi:10.1371/journal.pone.0127035

316. Kandeil A, Gomaa MR, Shehata MM, et al. Isolation and Characterization of a Distinct Influenza A Virus from Egyptian Bats. *Journal of Virology*. 2019-1-4 2019;93(2):e01059-18. doi:10.1128/JVI.01059-18

317. Yang W, Schountz T, Ma W. Bat Influenza Viruses: Current Status and Perspective. Review. *Viruses*. 2021-03-25 2021;13(4):547. doi:10.3390/v13040547

318. Kile DJ. Interview with Dr. James Kile - HPAI In: Schaeffer DM, editor. 2023.

319. Bodewes R, Bestebroer TM, van der Vries E, et al. Avian Influenza A(H10N7) Virus–Associated Mass Deaths among Harbor Seals. *Emerging Infectious Diseases*. 2015-4 2015;21(4):720-722. doi:10.3201/eid2104.141675

320. Hurt AC, Vijaykrishna D, Butler J, et al. Detection of Evolutionarily Distinct Avian Influenza A Viruses in Antarctica. *mBio*. 07/2014 2014;5(3)doi:10.1128/mBio.01098-14

321. Hurt AC, Su YCF, Aban M, et al. Evidence for the Introduction, Reassortment, and Persistence of Diverse Influenza A Viruses in Antarctica. *Journal of Virology*. 11/2016 2016;90(21):9674-9682. doi:10.1128/JVI.01404-16

322. Belser JA, Barclay W, Barr I, et al. Ferrets as Models for Influenza Virus Transmission Studies and Pandemic Risk Assessments. *Emerging Infectious Diseases*. 2018-6 2018;24(6):965-971. doi:10.3201/eid2406.172114

323. CDC. U.S. Influenza Surveillance: Purpose and Methods. Updated 2021-10-18T05:28:52Z. https://www.cdc.gov/flu/weekly/overview.htm

324. CDC. CDC Interim Guidance for Workers who are Employed at Commercial Swine Farms: Preventing the Spread of Influenza A Viruses | CDC. Updated 2023-06-06T02:09:56Z. https://www.cdc.gov/flu/swineflu/guidance-commercial-pigs.htm

325. Dr. Joni Schefter DSH. Interview with Dr. Schefter and Dr. Holzbauer (MN). In: Schaeffer DM, editor. 2023.

326. USDA. Public Health Monitoring Plan for USDA/APHIS Responders to Detections of Avian Influenza Virus in Poultry. https://www.aphis.usda.gov/animal_health/downloads/animal_diseases/ai/ai-monitoring-plan.pdf

327. CDC. Information for People Exposed to Birds Infected with Avian Influenza Viruses | Avian Influenza (Flu). Updated 2022-03-10T04:04:46Z. https://www.cdc.gov/flu/avianflu/h5/infected-birds-exposure.htm

328. CDC. International Health Regulations (IHR) | Division of Global Health Protection | Global Health. Updated 2020-06-01T08:12:31Z. https://www.cdc.gov/globalhealth/healthprotection/ghs/ihr/index.html

329. Paes B, Mitchell I, Li A, Lanctot KL. Respiratory hospitalizations and respiratory syncytial virus prophylaxis in special populations. *Eur J Pediatr*. May 2012;171(5):833-41. doi:10.1007/s00431-011-1654-8

330. CDC. National Respiratory and Enteric Virus Surveillance System | CDC. Updated 2022-01-25T10:36:06Z. https://www.cdc.gov/surveillance/nrevss/index.html

331. Koon K, Sanders CM, Green J, et al. Co-detection of Pandemic (H1N1) 2009 Virus and Other Respiratory Pathogens - Volume 16, Number 12—December 2010 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. 2010 2010;doi:10.3201/eid1612.091697

332. Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. *The Journal of Infection*. 2020-8 2020;81(2):266-275. doi:10.1016/j.jinf.2020.05.046

333. Rizzo KR, Hoover C, Jain S, et al. Influenza and SARS-CoV-2 Co-infections in California, USA, September 2020–April 2021 - Volume 27, Number 11—November 2021 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. 2021;doi:10.3201/eid2711.211129

334. Epperson S. Update: Influenza Activity — United States and Worldwide, May 19–September 28, 2019, and Composition of the 2020 Southern Hemisphere Influenza Vaccine. *MMWR Morbidity and Mortality Weekly Report*. 2019 2019;68doi:10.15585/mmwr.mm6840a3

335. Olsen SJ. Decreased Influenza Activity During the COVID-19 Pandemic — United States, Australia, Chile, and South Africa, 2020. *MMWR Morbidity and Mortality Weekly Report*. 2020 2020;69doi:10.15585/mmwr.mm6937a6

336. CDC. Preliminary In-Season 2021-2022 Flu Burden Estimates. Updated 2022-01-28. https://www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm

337. CDC. FluSight: Flu Forecasting. Updated 2021-12-16. https://www.cdc.gov/flu/weekly/flusight/index.html

338. CDC. Prevent Seasonal Flu. Updated 2021-11-18. https://www.cdc.gov/flu/prevent/index.html

339. CDC. How Flu Spreads. Updated 2018-08-27. https://www.cdc.gov/flu/about/disease/spread.htm

340. CDC. Novel Influenza a Virus Infections 2014 Case Definition. 2014. Accessed 2021-12-17 02:50:19. https://ndc.services.cdc.gov/case-definitions/novel-influenza-a-virus-infections-2014/

341. CDC. Evaluation of Rapid Influenza Diagnostic Tests for Influenza A (H3N2)v Virus and Updated Case Count — United States, 2012. *MMWR Morb Mortal Wkly Rep*. 2012 2012;61

342. CDC. Update: Influenza A (H3N2)v Transmission and Guidelines — Five States, 2011. *MMWR Morb Mortal Wkly Rep*. 1/6/2012 2012;60

343. CDC. Reported Human Infections with Avian Influenza A Viruses | Avian Influenza (Flu). Updated 2023-01-27T07:11:48Z. https://www.cdc.gov/flu/avianflu/reported-human-infections.htm

344. Liu D, Shi W, Shi Y, Wang D, Xiao H. Origin and diversity of novel avian influenza A H7N9 viruses causing human infection: phylogenetic, structural, and coalescent analyses. *Lancet*. 2013;doi:https://doi.org/10.1016/S0140-6736(13)60938-1

345. WHO. Monthly risk assessment summary: Influenza. https://www.who.int/teams/global-influenza-programme/avian-influenza/monthly-risk-assessment-summary

346. WHO. Influenza at the human-animal interface Summary and risk assessment, from 6 to 26 January 2023. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza-at-the-human-animal-interface-summary-and-assessment--from-6-to-26-january-2023.pdf?sfvrsn=abc6faf5_1&download=true

347. WHO. Global Influenza Programme. Updated 2022. https://www.who.int/teams/global-influenza-programme

348. CDC. Past Reported Global Human Cases with Highly Pathogenic Avian Influenza A(H5N1) (HPAI H5N1) by Country, 1997-2023 | Avian Influenza (Flu). Updated 2023-02-28T10:34:16Z. https://www.cdc.gov/flu/avianflu/chart-epi-curve-ah5n1.html

349. CDC. Highlights in the History of Avian Influenza (Bird Flu) Timeline – 2020-2023 | Avian Influenza (Flu). Updated 2023-02-27T06:28:13Z. https://www.cdc.gov/flu/avianflu/timeline/avian-timeline-2020s.htm

350. WHO. Influenza at the human-animal interface summary and assessment, January 2022. Updated 1/2022. https://cdn.who.int/media/docs/default-source/influenza/influenza_summary_ira_ha_interface_march_2022.pdf?sfvrsn=d1a866da_1&download=true

351. WHO. Monthly risk assessment summary. https://www.who.int/teams/control-of-neglected-tropical-diseases/lymphatic-filariasis/morbidity-management-and-disability-prevention/global-influenza-programme

352. WHO. Influenza at the human-animal interface summary and assessment, August 2021. Updated 8/8/2021. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_08_08_2021.pdf?sfvrsn=5aa110_5&download=true

353. WHO. Influenza at the human-animal interface Summary and assessment, from 8 April to 13 May 2022. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_may_2022.pdf?sfvrsn=6b4b3e20_1&download=true

354. WHO. Influenza at the human-animal interface Summary and assessment, from 14 May to 27 June 2022. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza-at-the-human-animal-interface-summary-and-assessment--from-14-may-to-27-june-2022.pdf?sfvrsn=bdf329be_3&download=true

355. WHO. Influenza at the human-animal interface Summary and assessment, from 22 January to 1 March 2022. https://cdn.who.int/media/docs/default-source/influenza/influenza_summary_ira_ha_interface_march_2022.pdf?sfvrsn=d1a866da_1&download=true

356. WHO. Influenza at the human-animal interface Summary and risk assessment, from 6 October to 11 November 2022. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza-at-the-human-animal-interface-summary-and-assessment--from-6-october-to-11-november-2022.pdf?sfvrsn=db9a4370_1&download=true

357. WHO. Influenza at the human-animal interface Summary and risk assessment, from 12 November 2022 to 5 January 2023. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza-at-the-human-animal-interface-summary-and-assessment--from-12-november-to-5-january-2023.pdf?sfvrsn=8382d727_1&download=true

358. WHO. Influenza at the human-animal interface Summary and risk assessment, from 28 June to 30 August 2022. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_aug_2022.pdf?sfvrsn=77e3e28e_1&download=true

359. WHO. Influenza at the human-animal interface Summary and risk assessment, from 31 August to 5 October 2022. https://cdn.who.int/media/docs/default-source/2021-dha-docs/influenza-at-the-human-animal-interface-summary-and-assessment--from-31-august-to-5-october-2022.pdf?sfvrsn=c67e1ab8_1&download=true

360. WHO. Influenza at the human-animal interface summary and assessment, December 2021. Updated 12/2021. https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_jan_2022.pdf?sfvrsn=1893dd9f_5&download=true

361. Oliver I, Roberts J, Brown CS, et al. A case of avian influenza A(H5N1) in England, January 2022. Text. European Centre for Disease Prevention and Control. Updated 2022/02/03. https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.5.2200061

362. CDC. Technical Report: Highly Pathogenic Avian Influenza A(H5N1) Viruses. Updated 2023-03-17T04:34:49Z. https://www.cdc.gov/flu/avianflu/spotlights/2022-2023/h5n1-technical-report.htm

363. CDC. U.S. Case of Human Avian Influenza A(H5) Virus Reported. https://www.cdc.gov/media/releases/2022/s0428-avian-flu.html

364. USDA. 2022 Confirmations of Highly Pathogenic Avian Influenza in Commercial and Backyard Flocks. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian/avian-influenza/hpai-2022

365. WHO. Assessment of risk associated with recent influenza A(H5N1) clade 2.3.4.4b viruses. https://cdn.who.int/media/docs/default-source/influenza/avian-and-other-zoonotic-influenza/h5-risk-assessment-dec-2022.pdf?sfvrsn=a496333a_1&download=true

366. Additive F. Global Poultry Industry and Trends. https://www.feedandadditive.com/global-poultry-industry-and-trends/

367. Baldwin M, Reider H. Interview with the NPIP Coordinator for CO and the State Public Health Veterinarian for CO. 2021.

368. HPAI Response Plan: The Red Book (Updated May 2017) (USDA) 224 (2017).

369. USFWS. U.S. Fish & Wildlife Service - Migratory Bird Program | Conserving America's Birds. https://www.fws.gov/program/migratory-birds

370. Diskin ER, Friedman K, Krauss S, et al. Subtype Diversity of Influenza A Virus in North American Waterfowl: a Multidecade Study. *Journal of Virology*. 2020-5-18 2020;94(11):e02022-19. doi:10.1128/JVI.02022-19

371. Pearson GL. Field Manual of Wildlife Diseases: General Field Procedures and Diseases of Birds. *Journal of Wildlife Diseases*. 01/2001 2001;37(1):208-211. doi:10.7589/0090-3558-37.1.208

372. Nations FaAOotU. EMPRES-i. https://www.fao.org/home/en

373. Authority EFS. Avian influenza: unprecedented number of summer cases in Europe. https://www.efsa.europa.eu/en/news/avian-influenza-unprecedented-number-summer-cases-europe#:~:text=The%20ongoing%20HPAI%20season%20has%20produced%20the%20largest,3%2C573%20HPAI%20events%20were%20recorded%20in%20wild%20birds.

374. Swayne D. *HPAI OneHealth Committee Presentation*. 2022. 8/23/22.

375. Adlhoch C, Fusaro A, Gonzales J, Kuiken T, Marangon S. Avian influenza overview March - June 2022. *EFSA journal*. 08/06/2022 2022;20(8)doi:10.2903/j.efsa.2022.7415

376. Caliendo V, Lewis NS, Pohlmann A, Baillie SR, Banyard AC, Beer M. Transatlantic spread of highly pathogenic avian influenza H5N1 by wild birds from Europe to North America in 2021. *Scientific Reports*. 2022;12doi:https://doi.org/10.1038%2Fs41598-022-13447-z

377. Bevins SN, Shriner SA, Cumbee JC, Dilione KE, Douglass KE. Intercontinental Movement of Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4 Virus to the United States, 2021 - Volume 28, Number 5—May 2022 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. April 19, 2022 2022;

378. Xu W, Berhane Y, Dubé C, et al. Epidemiological and Evolutionary Inference of the Transmission Network of the 2014 Highly Pathogenic Avian Influenza H5N2 Outbreak in British Columbia, Canada. *Scientific reports*. 08/04/2016 2016;6doi:10.1038/srep30858

379. Lab TC. The Basics of Bird Migration: How, Why, and Where. Updated 2021-08-01. https://www.allaboutbirds.org/news/the-basics-how-why-and-where-of-bird-migration/

380. USDA. Epidemiologic and Other Analyses of HPAI Affected Poultry Flocks July 2022 Interim Report. https://www.aphis.usda.gov/sites/default/files/epi-analyses-hpai-poultry-july2022.pdf

381. USDA. 2022-2023 Detections of Highly Pathogenic Avian Influenza in Wild Birds. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian/avian-influenza/hpai-2022/2022-hpai-wild-birds

382. USDA. 2022-2023 Confirmations of Highly Pathogenic Avian Influenza in Commercial and Backyard Flocks. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian/avian-influenza/hpai-2022/2022-hpai-commercial-backyard-flocks

383. Moffitt JC, Carol; Bevins, Sarah; Padilla, Samantha. Highly Pathogenic Avian Influenza (HPAI) and International Trade. 2023:

384. Lesley C. 5 ways 2020 changed the backyard chicken industry. @thepoultrysite. https://www.thepoultrysite.com/articles/5-ways-2020-changed-the-backyard-chicken-industry

385. CDC. H5N1 Bird Flu Detections across the United States (Backyard and Commercial) | Avian Influenza (Flu). @CDCgov. Updated 2023-03-08T06:19:20Z. https://www.cdc.gov/flu/avianflu/data-map-commercial.html

386. Rijks JM, Hesselink H, Lollinga P, et al. Highly Pathogenic Avian Influenza A(H5N1) Virus in Wild Red Foxes, the Netherlands, 2021. *Emerging Infectious Diseases*. 2021-11 2021;27(11):2960-2962. doi:10.3201/eid2711.211281

387. Vreman S, Kik M, Germeraad E, Heutink R, Harders F, Spierenburg M. Zoonotic Mutation of Highly Pathogenic Avian Influenza H5N1 Virus Identified in the Brain of Multiple Wild Carnivore Species. *Pathogens (Basel, Switzerland)*. 01/20/2023 2023;12(2)doi:10.3390/pathogens12020168

388. Wang P. Explosion of sea lion deaths in Peru amid deadly bird flu outbreak. 1678641346. https://www.msn.com/en-us/health/medical/explosion-of-sea-lion-deaths-in-peru-amid-deadly-bird-flu-outbreak/ar-AA18iqXa

389. Agüero M, Monne I, Sánchez A, et al. Highly pathogenic avian influenza A(H5N1) virus infection in farmed minks, Spain, October 2022. Text. *European Centre for Disease Prevention and Control*. 2023/01/19 2023;doi:doi:10.2807/1560-7917.ES.2023.28.3.2300001

390. Keawcharoen J, Oraveerakul K, Kuiken T, et al. Avian Influenza H5N1 in Tigers and Leopards - Volume 10, Number 12—December 2004 - Emerging Infectious Diseases journal - CDC. *Emerg Infect Dis*. April 14, 2011 2011;

391. Hu T, Zhao H, Zhang Y, et al. Fatal influenza A (H5N1) virus Infection in zoo-housed Tigers in Yunnan Province, China. OriginalPaper. *Scientific Reports*. 2016-05-10 2016;6(1):1-9. doi:doi:10.1038/srep25845

392. USDA. 2022-2023 Detections of Highly Pathogenic Avian Influenza in Mammals. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian/avian-influenza/hpai-2022/2022-hpai-mammals

393. CDC. How Infected Backyard Poultry Could Spread Bird Flu to People. https://www.cdc.gov/healthypets/pets/farm-animals/backyard-poultry.html

394. USDA. USDA Questions and Answers: Biology of Avian Influenza and Recent Outbreaks. Updated 5/2015. https://www.usda.gov/sites/default/files/documents/avian-influenza-united-states-qa.pdf

395. WHO. Influenza at the human-animal interface summary and assessment, October 2021. Accessed 10/2021, https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_23_12_2021.pdf?sfvrsn=5a707c7_10&download=true

396. WOAH. Equine influenza. *WOAH - World Organisation for Animal Health* blog. 2023. Accessed 2021-12-17 14:46:31. https://www.woah.org/en/home/

397. WOAH. Terrestrial Code Online Access. *WOAH - World Organisation for Animal Health* blog. 2021. Accessed 2021-10-09 21:54:54. https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/

398. WOAH. Infection with High Pathogenicity Avian Influenza Viruses. *WOAH - World Organisation for Animal Health* blog. 2021. Accessed 2022-01-30 15:09:01. https://www.woah.org/en/disease/avian-influenza/

399. Hennefent DA. Interview with Dr. Hennefent. In: Schaeffer DM, editor. 2023.

400. Hongbo Zhang YY, Yan Li, Jianjun Chen, and Ze Chen. Evidence for Water-Borne Transmission of Highly Pathogenic Avian Influenza H5N1 Viruses. *Frontiers in Microbiology*. 5/26/22 2022;

401. USDA. Defend the Flock - Signs of Illness. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian/defend-the-flock-program/outbreak-illness/outbreak-illness

402. USDA. Defend the Flock - Biosecurity 101. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian/defend-the-flock-program/outbreak-illness/outbreak-illness

403. CDC. Recommendations for Worker Protection and Use of Personal Protective Equipment (PPE) to Reduce Exposure to Novel Influenza A Viruses Associated with Severe Disease in Humans | Avian Influenza (Flu). Updated 2022-03-08T03:43:09Z. https://www.cdc.gov/flu/avianflu/h5/worker-protection-ppe.htm

404. Bennett DJ. Interview with Dr. Bennett (NY State). In: Schaeffer DM, editor. 2023.

405. Castrodale DL. Interview with Dr. Castrodale (AK). In: Schaeffer DM, editor. 2023.

406. Radcliffe DR. Interview with Dr. Radcliffe (SC/CSTE). In: Schaeffer DM, editor. 2023.

407. Jagne, Bennett, Dacvpm, Collins. Live Bird Markets of the Northeastern United States. *Delaware journal of public health*. 01/21/2021 2021;7(1)doi:10.32481/djph.2021.01.009

408. CDC. Prevention and Antiviral Treatment of Bird Flu Viruses in People | Avian Influenza (Flu). Updated 2023-02-01T06:16:15Z. https://www.cdc.gov/flu/avianflu/prevention.htm#anchor_1647619425331

409. CDC. What To Know About Bird Flu. https://www.cdc.gov/flu/pdf/avianflu/Bird-Flu-Exposure-Handout.pdf

410. Gangurde H, Gulecha VS, Borkar VS, Mahajan MS, Khandare R, Mundada A. Swine Influenza A (H1N1 Virus): A pandemic disease. *Systematic Reviews in Pharmacy*. July 1, 2011 2011;2:110-124. doi:10.4103/0975-8453.86300

411. National Surveillance Plan for Swine Influenza Virus in Pigs (USDA APHIS) 27 (2010).

412. WOAH. Diseases, Infections, and Infestations Listed by the WOAH. *WOAH - World Organisation for Animal Health* blog. 2021. Accessed 2022-01-29 20:53:44. http://www.animalhealthsurveillance.agriculture.gov.ie/woahlisteddiseases/#:~:text=WOAH%20Listed%20Diseases%201%20Anthrax%202%20Crimean%20Congo,virus%208%20Infection%20with%20bluetongue%20virus%20More%20items

413. Health W-WOfA. Swine influenza. https://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/SWINE_INFLUENZA.pdf

414. Duwell MM. Influenza A(H3N2) Variant Virus Outbreak at Three Fairs — Maryland, 2017. *MMWR Morbidity and Mortality Weekly Report*. 2018 2018;67doi:10.15585/mmwr.mm6742a1

415. Komadina N, McVernon J, Hall R, Leder K. A Historical Perspective of Influenza A(H1N2) Virus. *Emerging Infectious Diseases*. 2014-1 2014;20(1):6-12. doi:10.3201/eid2001.121848

416. Karasin AI, Olsen CW, Anderson GA. Genetic Characterization of an H1N2 Influenza Virus Isolated from a Pig In Indiana. *Journal of Clinical Microbiology*. June 1, 2000 2000;38(6):2453-2456. doi:10.1128/JCM.38.6.2453-2456.2000

417. Olsen CW, Brammer L, Easterday BC, et al. Serologic Evidence of H1 Swine Influenza Virus Infection in Swine Farm Residents and Employees. *Emerging Infectious Diseases journal*. August 2002 2002;8(8)doi:10.3201/eid0808.010474

418. Pantin-Jackwood M, Wasilenko JL, Spackman E, Suarez DL, Swayne DE. Susceptibility of turkeys to pandemic-H1N1 virus by reproductive tract insemination. *Virology Journal*. February 3, 2010 2010;7(1):27. doi:10.1186/1743-422X-7-27

419. Suarez DL, Woolcock PR, Bermudez AJ, Senne DA. Isolation from Turkey Breeder Hens of a Reassortant H1N2 Influenza Virus with Swine, Human, and Avian Lineage Genes. *Avian Diseases*. 2002/01 2002;46(1):111-121. doi:10.1637/0005-2086(2002)046[0111:IFTBHO]2.0.CO;2

420. Signs K. Notes and comments from Dr. Kimberly Signs. 2022.

421. Payungporn S, Crawford PC, Kouo TS, et al. Influenza A Virus (H3N8) in Dogs with Respiratory Disease, Florida. *Emerging Infectious Diseases*. 2008-6 2008;14(6):902-908. doi:10.3201/eid1406.071270

422. Gardiner J. Vaccination Guidelines for Dogs and Cats. Updated 2019-03-27T14:25:49-07:00. https://healthtopics.vetmed.ucdavis.edu/health-topics/feline/vaccination-guidelines-dogs-and-cats

423. USDA. Serologic Prevalence of Canine Influenza (H3N8) in Shelter Dogs in Philadelphia. Updated 2011. https://portal.nifa.usda.gov/web/crisprojectpages/0216838-serologic-prevalence-of-canine-influenza-h3n8-in-shelter-dogs-in-philadelphia.html

424. Jones JC, Sonnberg S, Koçer ZA, et al. Possible Role of Songbirds and Parakeets in Transmission of Influenza A(H7N9) Virus to Humans. *Emerging Infectious Diseases journal*. March 2014 2014;20(3)doi:10.3201/eid2003.131271

425. AVMA. Avian Influenza in Companion Animals. Updated 2021. https://www.avma.org/resources-tools/animal-health-and-welfare/animal-health/avian-influenza/avian-influenza-companion-animals

426. CDC. Zika Virus. Updated 2014-11-05T18:00:00-05:00. https://www.cdc.gov/zika/index.html

427. CDC. Are We Prepared? Updated 2017-12-13. https://www.cdc.gov/orr/areweprepared.htm

428. CDC. 2014-2016 Ebola Outbreak in West Africa | History | Ebola (Ebola Virus Disease) | CDC. Updated 2020-03-17T07:17:33Z. https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html

429. CDC. Human Coronavirus Types | CDC. Updated 2021-03-17T07:03:15Z. https://www.cdc.gov/coronavirus/types.html

430. Noor R, Maniha SM. A brief outline of respiratory viral disease outbreaks: 1889–till date on the public health perspectives. *VirusDisease*. 2020-12 2020;31(4):441-449. doi:10.1007/s13337-020-00628-5

431. NASPHV. Compendium of Measures to Prevent Disease Associated with Animals in Public Settings, 2011. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6004a1.htm

432. Sandbulte M. Optimal Use of Vaccines for Control of Influenza A Virus in Swine. *Vaccines (Basel)*. 2015;3(1)doi:10.3390/vaccines3010022

433. WOAH. Bird flu has been spreading among US cows for months, RNA reveals. Updated April 2024. https://www.nature.com/articles/d41586-024-01256-5.

434. USDA APHIS. Detection of Highly Pathogenic Avian Influenza (H5N1) in Dairy Herds: FAQ. Updated April 2024. https://www.aphis.usda.gov/sites/default/files/hpai-dairy-faqs.pdf.

435. USDA APHIS. Highly Pathogenic Avian Influenza (HPAI) Detections in Livestock. Updated May 2024. https://www.aphis.usda.gov/sites/default/files/hpai-dairy-faqs.pdf.

436. CDC. Current H5N1 Bird Flu Situation in Dairy Cows. Updated 2024. https://www.cdc.gov/flu/avianflu/mammals.htm.

437. WHO. Influenza at the human-animal-interface and assessment. Updated May 2024. https://www.who.int/teams/global-influenza-programme/avian-influenza.

438. CDC. Avian Influenza A(H5N1) Situation Update and CDC Activities. Updated April 2024. https://www.who.int/teams/global-influenza-programme/avian-influenza.

439. CDC. Highly Pathogenic Avian Influenza A(H5N1) Virus Reported in a Person in the U.S. Updated April 2024. https://www.cdc.gov/media/releases/2024/p0401-avian-flu.html.

440. CDC. Novel Influenza A Virus Infections. Updated 2024. https://gis.cdc.gov/grasp/fluview/Novel_Influenza.html.

441 WHO. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2024. Updated May 2024. https://cdn.who.int/media/docs/default-source/influenza/h5n1-human-case-cumulative-table/2024_may_tableh5n1.pdf?sfvrsn=6ab0fe24_3&download=true