HUMAN EMERGING RESPIRATORY PATHOGENS BULLETIN

MONTHLY SITUATIONAL ANALYSIS OF EMERGING RESPIRATORY DISEASES AFFECTING HUMANS

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IN THIS BULLETIN

COVID-19 UPDATE

On December 31, 2019, cases of a pneumonia of unknown etiology were reported in Wuhan, China. These cases have since been determined to be due to a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19). On January 30, 2020, the World Health Organization (WHO) first declared the outbreak a Public Health Emergency of International Concern (PHEIC). On March 11, 2020, the WHO characterized the outbreak as a global pandemic. The WHO Director-General convened the International Health Regulations (IHR) Emergency Committee (EC) on COVID-19 ten (10) times from 2020 to date, continually assessing that COVID-19 constitutes a PHEIC.

The Public Health Agency of Canada is monitoring the situation closely. For the most up-to-date information, please visit: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html

UPDATE ON HUMAN EMERGING RESPIRATORY PATHOGEN PUBLIC HEALTH EVENTS (AS OF JANUARY 31, 2022)[1]

NOVEL INFLUENZA[1]	[N CUMULATIVE CASES[2] (DEATHS), CFR%[3]]
A(H7N9)	[1,568 (615), 39%]
A(H5N1)	[882 (462), 52%]
A(H9N2)	[91 (2), 2%]
A(H5N6)	[66 (29), 44%]
A(H5N8)	[7 (0), 0%]
A(H7N4)	[1 (0), 0%]
A(H1N2)[4]	[2 (0), 0%]
A(H3N2)v	[441 (1), <1%]
A(H1N2)v	[39 (0), 0%]
A(H1N1)v	[38 (0), 0%]
A(H1NX)v[5]	[1 (0), 0%]
A(H10N3)	[1 (0), 0%]
Eurasian avian-like A(H1N1)v	[10 (0), 0%]
MERS-CoV[1]	
Global case count	[2,576 (880), 34%]
Saudi Arabia	[2,178 (802), 37%]

[1]**Date of 1st Reported Case of Human Infection:** MERS-CoV: February 2013 (retrospective case finding September 2012). A(H7N9): March 2013. A(H5N1): 1997. A(H9N2): 1998. A(H5N6): 2014. A(H5N8): December 2020. A(H7N4): February 2018. A(H1N2): March 2018. A(H3N2)v with M gene from pH1N1: 2011. A(H1N2)v: 2005. A(H1N1)v: 2005. EA A(H1N1): 1986, but the above table counts cases from January 2021. A/Denmark/1/2021: February 2021
[2]**Cumulative Case Counts:** updated using data reported by the World Health Organization (avian and swine influenza, MERS CoV), and the United States Centers for Disease Control and Prevention (US CDC) (swine influenza).
[3]**Case Fatality Rate (CFR):** the proportion of cases that resulted in death. For events with active cases, may be updated retrospectively as final disposition is known.
[4]**A(H1N2)**: virus is a seasonal reassortant of the A(H1N1)pdm09 and A(H3N2) seasonal strains.
[5]**A(H1Nx)v:** virus is a novel influenza A(H1) virus with pending neuraminidase results.

Public Health Agency of Canada Agence de la santé publique du Canada

Canada

AVIAN INFLUENZA UPDATES

AVIAN INFLUENZA A(H9N2)

Five (5) new cases of avian influenza A(H9N2) were reported in January 2022, all from China. The cases range in age from 3 years old to 14 years old. Most (3/5; 60%) of the reported cases are female. They were reported from four (4) different provinces: Anhui, Jiangsu, Hubei, and Guangxi. All cases had history of poultry exposure prior to illness onset, developed mild illness, and had already recovered at the time of report.

Including these cases, 25 human cases of A(H9N2) developed illness in 2021, with the majority (24/25; 96%) of cases reported out of China. No cases have yet been reported that had illness onset in 2022. No cases have been reported in Canada. Since the emergence of this virus in the human population in 1998, 91 cases have been reported worldwide, with a case fatality rate (CFR) of 2%.

AVIAN INFLUENZA A(H5N1)

On January 6, 2022, the United Kingdom (UK) Health Security Agency (UKHSA) reported one (1) human case of avian influenza A(H5NX), which was later confirmed to be A(H5N1). This case was detected in southwest England. The case is over 70 years old, asymptomatic, and was non-infectious at the time of report. The case was exposed to A(H5N1) via infected domestic birds kept on the residence prior to illness onset. The birds were culled and the case was tested out of precaution. No onward transmission of the virus was identified through case contact follow-up.

In total, 882 human cases of A(H5N1) have been reported globally, with a CFR of 52%. Canada (Alberta) has reported one single fatal case of A(H5N1) in 2014, in a resident returning from travel in China. No cases have yet been reported in 2022.

SWINE INFLUENZA UPDATES

SWINE ORIGIN INFLUENZA A(H1N2)v

The most recent cases of swine origin influenza A(H1N2)v were reported in November 2021 from the US and Canada.

Three A(H1N2)v detections have been reported in Canadian residents since reporting began in 2005. A total of 39 cases have been reported globally since 2005, with a 0% case fatality rate. There have been 11 A(H1N2)v cases reported globally in 2021.

SWINE ORIGIN INFLUENZA A(H3N2)v

The most recent case of swine origin influenza A(H3N2)v was reported in October 2021 from the US.

Two A(H3N2)v detections have been reported in Canadian residents since reporting began in 2005, with the latest case reported in June 2021. Globally, 441 A(H3N2)v cases have been reported since 2005, with <1% case fatality rate. There have been 5 A(H3N2)v cases reported worldwide in 2021.

SWINE ORIGIN INFLUENZA A(H1N1)v

On January 18, 2022, Denmark reported one (1) human case of swine origin influenza virus (subtype A/H1pdm09N1av-like) to the WHO. The case developed illness on November 23, 2021, after occupational exposure to swine. He was admitted to the ICU. No other cases were detected through case contact follow-up.

Two A(H1N1)v detections have been reported in Canadian residents since reporting began in 2005, with the latest case reported in April 2021. Globally, 38 human cases of A(H1N1)v have been reported since 2005, with no associated fatalities. There have been seven (7) A(H1N1)v cases reported worldwide in 2021 and one (1), including this case, reported in 2022.

MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS (MERS-COV) UPDATE

The most recent cases of MERS-CoV were reported in December 2021 from the Kingdom of Saudi Arabia. Nineteen cases of MERS-CoV have been reported worldwide in 2021 [eight (8) of them fatal], with 17 of these cases reported from Saudi Arabia and two (2) from the United Arab Emirates. A total of 2,576 laboratory-confirmed cases of MERS-CoV, including 880 deaths, have been reported globally since 2012 by the WHO (CFR: 34%). No cases have been reported in Canada.

IN DEPTH ANALYSIS

HUMAN RESPIRATORY DISEASE ASSOCIATED WITH AVIAN INFLUENZA A(H5N6)

Eight (8) human cases of avian influenza A(H5N6) were reported in January 2022, all from China. Including these cases, a total of 66 laboratory-confirmed human cases of avian influenza A(H5N6), including at least 29 deaths, have been reported globally since 2014. Further information can be found below.

RISK TO CANADA

The goal of this in-depth analysis is to summarize the current available information on the epidemiology of human infection with avian influenza A(H5N6) [A(H5N6)].

Since the emergence of A(H5N6) in the human population in 2014 and as of February 1st, 2022, 66 human cases have been reported from the People's Republic of China (China) and Lao People's Democratic Republic (Lao PDR). No cases of A(H5N6) have been reported in Canadian residents. Although the current available information suggests this virus does not have the ability to transmit easily among humans, additional sporadic human cases of A(H5N6) are expected to be reported in regions where A(H5N6) continues to circulate in wild and domestic birds.

Risk assessments for avian influenza A(H5N6) have been undertaken by several institutions, including the World Health Organization (WHO), the United States (US) Centers for Disease Control and Prevention (CDC) [using the Influenza Risk Assessment Tool (Tool)], and the United Kingdom (UK). A risk assessment for A(H5N6) has not been completed for Canada.

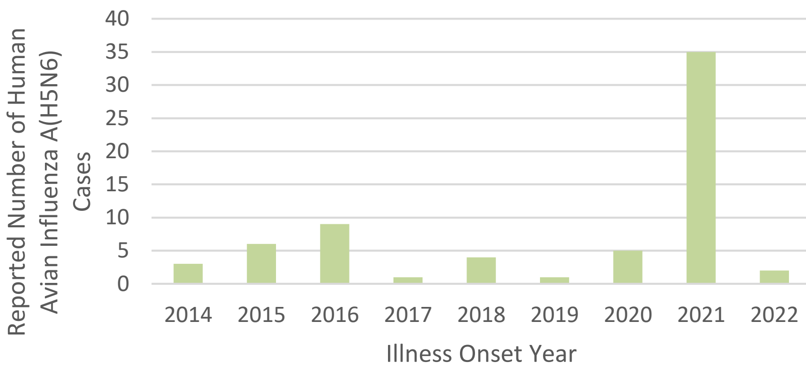
Guidance related to avian influenzas like A(H5N6), including the Public Health Agency of Canada (PHAC)'s Severe Acute Respiratory Infection (SARI) Case Report Form, laboratory guidance for SARI investigations, epidemiologic guidance for SARI investigations, biosecurity guidance for H5/H7/H9 influenzas, surveillance guidance for avian influenza in humans [specific to A(H7N9) but can be applied to A(H5N6)], and the Canadian Pandemic Influenza Planning (CPIP) Guidance are available online.

BACKGROUND

Avian influenza viruses (AIVs) can affect several species of domestic or wild birds. Based on their pathogenicity, AIVs are classified as either low pathogenicity avian influenza (LPAI) or highly pathogenic avian influenza (HPAI). Over the past two (2) decades, AIVs have become enzootic in domestic poultry populations in many Asian countries (1). Today, China is recognized as a hotspot for the emergence, transmission, and dissemination of AIVs due to their widespread persistence, the nature and growth of the poultry production industry, live poultry trading, and the mixing of host species in live bird markets (LBMs) (2) (3) (4).

Avian influenza A(H5N6) is a HPAI virus that can cause severe disease and high mortality in infected poultry (3). Outbreaks of A(H5N6) were reported in birds in Laos, China, and Vietnam prior to the report of the first human case in China in 2014 (5). Human cases of A(H5N6) have continued to be reported since, with a marked increase in detections in 2021 [Figure 1]. Although it is possible that this increase coincides with heightened surveillance and diagnostic systems resulting from the COVID-19 pandemic, other factors like the spread of AIVs in poultry populations likely also play a role in the increased number of cases (6).

Figure 1. Epidemiologic curve of human avian influenza A(H5N6) infections, by year of illness onset or report date, 2014-January 31, 2022 (n=66).



Note: Illness onset data were unavailable for three (3) cases; for these cases, report date data were utilized to create this figure. The cases included in this figure are cases reported up until January 31, 2022. Source: the Centre for Immunization and Respiratory Infectious Diseases (CIRID)'s International Monitoring and Assessment Tool (IMAT).

Further understanding of both the human and animal epidemiology of this disease is essential to characterize the risk of emergence and human health impact posed by this novel influenza virus. This in-depth analysis is based on a review of published literature, supplemented with a selected search of official organizational materials published by the WHO, US CDC, Hong Kong's Centre for Health Protection (Hong Kong CHP), and the World Organisation for Animal Health (OIE). Data from these sources were collated, verified, recorded in IMAT, and cleaned to conduct epidemiologic analyses on human cases of A(H5N6) reported globally.

VIROLOGICAL INFORMATION

Avian influenza A(H5N6) is a variant HPAI A(H5) virus belonging to novel clade 2.3.4.4 (7) (8). Genetic analysis of avian and human isolates from 2014-2021 confirm this virus is a reassortant AIV with hemagglutinin (HA) from clade 2.3.4.4 A(H5) viruses, and neuraminidase (NA) from H5N6, H6N6, H3N6, or H10N6 viruses. The internal genes are either from 2.3.4.4 A(H5) clade viruses, 2.3.2.1 A(H5) clade viruses, or H3N2, H3N8, H4N2, H6N6, H7N9 and H9N2 viruses [Figure 2] (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18) (19) (20) (21). The source species for the genes of these human isolates include chicken, goose, swan, duck, gulls, and humans (16) (17) (18) (19) (20) (21). Every A(H5N6) virus that was sequenced from human cases in China with an illness onset date after February 2021 (and prior to November 29, 2021) belonged to the 2.3.4.4b genetic clade, although one viral sequence from earlier in the year belonged to a different clade that had been commonly detected in birds up to that point (6).

Genetic signature analyses of A(H5N6) isolates indicate preferable binding to avian-like receptors (3) (4) (9) (22). Nevertheless, certain sequences also indicate associations with mammalian adaptations, such as increased human cell receptor binding (3) (4) (6) (9) (22). The diversity of AIVs circulating in China, along with continued interaction between host species, allows for continued reassortment of these viruses [Figure 2].

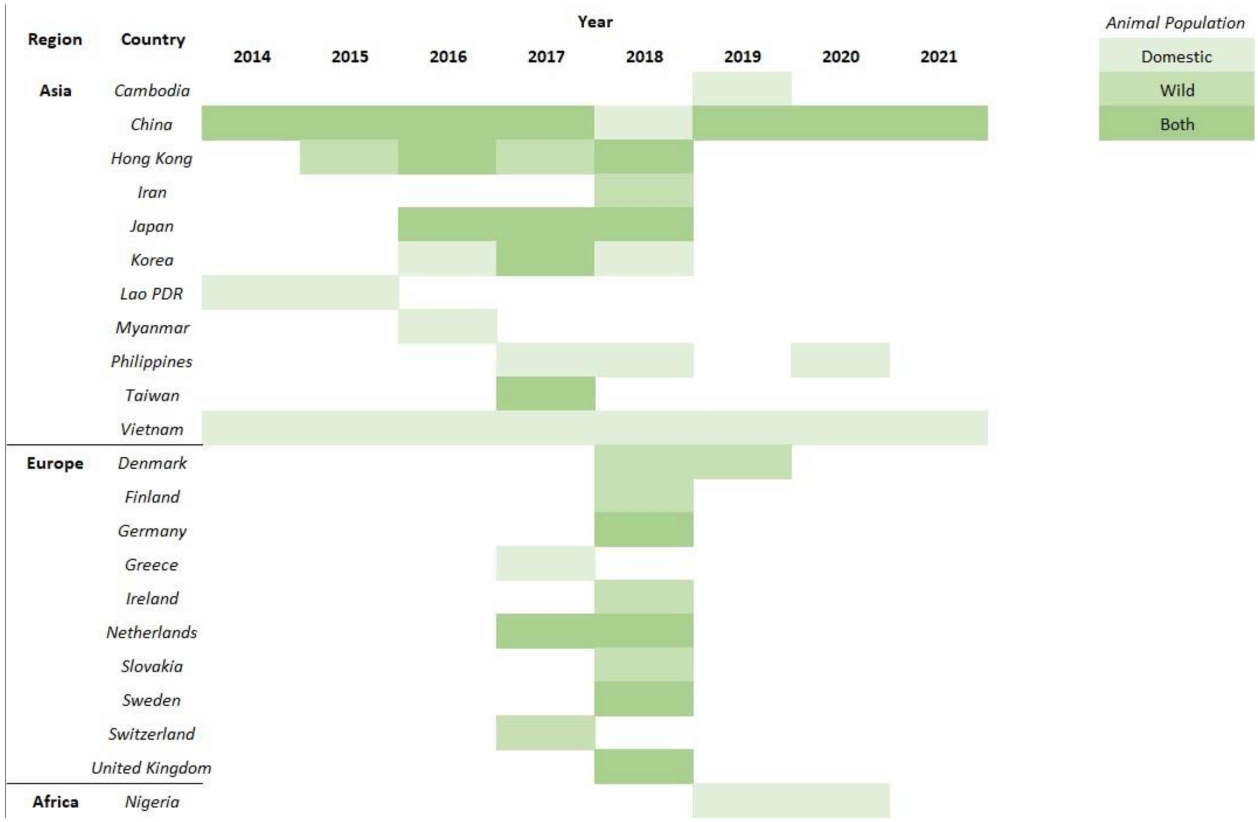
Figure 2. Schematic of genetic source of select human isolates of avian influenza A(H5N6) analyzed from 2014-2021.

Note: This figure, a hypothesis of genetic lineages for some human avian influenza A(H5N6) isolates, was completed using data from peer-reviewed published literature (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18) (19) (20) (21). It is not a comprehensive diagram and may contain incomplete information. Viruses are represented by circular shaped structures. The horizontal bars within the viruses in the diagram signify viral genes. From top to bottom, the eight (8) genes in each virus are: PB2, PB1, PA, HA, NP, NA, MP, and NS.

ANIMAL INFECTIONS AND ENVIRONMENTAL DETECTIONS

In 2014, HPAI A(H5N6) was detected in domestic and wild bird populations in Asia, from China, Vietnam, and Laos. Since then, widespread avian outbreaks have continued to be reported in bird populations worldwide, with detections reported to the OIE from 21 different countries in Asia, Europe, and Africa to date [Figure 3] (23).

Figure 3. Summary of animal outbreaks of avian influenza A(H5N6) reported to OIE, 2014-2021.



Note: This figure was created with data extracted from the OIE World Animal Health Information System (WAHIS) on December 16, 2021.

A(H5N6) has been detected in multiple environments. For instance, environmental samples of live poultry farming and trading places (including LBMs) revealed positive A(H5N6) swabs from chopping boards, sewage (including water used to clean slaughtered poultry, processing tools, and cages)/fecal samples, and poultry feeding/drinking sites (17) (18) (19) (24) (25). This virus has also been detected in residences (e.g. positive samples from backyard poultry, environments) of cases with domestic poultry or contact with birds (26).

EXPOSURE

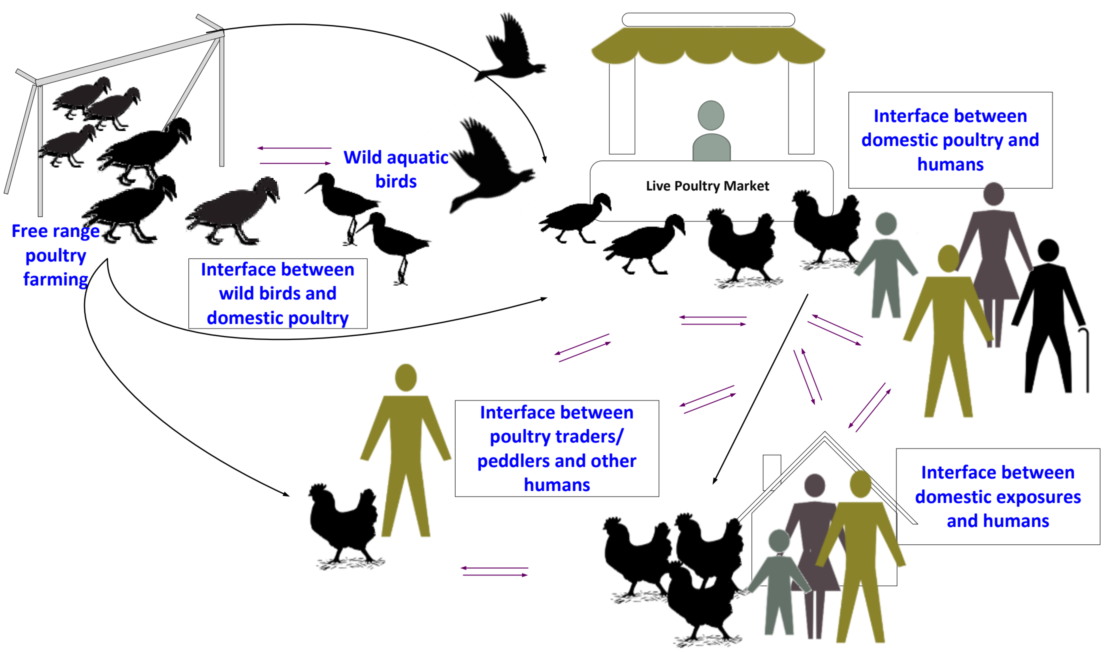
Modes of Transmission

Avian influenza A(H5N6) primarily infects birds, but also infects mammals including humans. This virus is transmitted from bird-to-bird through secretions and droppings (27). Asymptomatic transmission is also a possibility as some species of wild birds, such as ducks, can carry the virus and infect other birds without developing illness. Although avian influenza A(H5N6) rarely infects humans, transmission may occur through contact with contaminated environments or infected birds (27) (28). To date, there is no evidence of sustained human-to-human transmission.

Exposure Sources

Live Poultry Feeding and Trading Markets (LPFTMs) are considered a risk factor for human cases of various AIVs, including HPAI A(H5N6) (24). Exposure to birds through these environments may increase risk of A(H5N6) infection through direct or indirect contact with infected poultry (29). In fact, every case with known exposure information (53/53; 100%) reported indirect or direct contact with birds prior to illness onset, through LBMs, poultry workers, slain and cooked poultry, and/or domestic/backyard poultry (26). Epidemiological investigations have revealed positive H5 results from the backyards of several cases in China who kept domestic poultry or had wild birds frequent their residences. Confirmed human A(H5N6) cases have also been linked to local LPFTMs through genetic analysis and comparison of viral case and environmental samples [Figure 4] (19) (21) (24) (26). Workers with occupational exposures, such as poultry sellers, are at higher risk of positive serology and investigators have observed positive A(H5N6) serology specimens from poultry workers in the past (note: this does not constitute a positive case). They also noted an elevated risk exists for those aged ≥55 years and individuals exposed to sick or dead poultry (30). However, the risk of animal-to-human transmission is low in the presence of personal protective equipment (PPE) and other biosecurity and preventive measures such as antiviral prophylaxis after potential exposure (31).

Figure 4. Schematic of the transmission of avian influenza A(H5N6) from wild birds to humans.



Note: This figure, a schematic of AIV A(H5N6) transmission from wild birds to humans, was completed using data from peer-reviewed published literature (19) (21) (24) (26). It is not a comprehensive diagram and may contain incomplete information.

GLOBAL EPIDEMIOLOGY

Case Characteristics

While avian influenza A(H5N6) outbreaks in birds have been observed worldwide, avian-to-human transmission has only been detected in two (2) Asian countries. Since 2014, 66 human cases of A(H5N6) have been reported globally, all from China and Lao PDR. The median age of these cases was 50.5 years, with an age range of 1-81 years. Nine (9) (9/66, 14%) reported cases were children <18 years of age [Table 1]. Half (33/66; 50%) of the cases were males [Table 1]. At least 29 cases have died [case fatality rate (CFR): 44%] and of the cases with unknown outcome but available disposition data, 84% (21/25) were in critical or severe condition at the time of last report. All cases with known exposure data (53/53; 100%) reported contact with birds prior to illness onset. Of the 22 cases with reported occupational background, 82% (18/22) had obvious associations with agricultural work and/or poultry exposure as farmers (15/22; 68%) or dealers with contact with Live Bird Markets (LBMs) (3/21; 14%).

Table 1. Descriptive Characteristics of Cases by Sex and Age Groups, 2014 – January 31, 2022

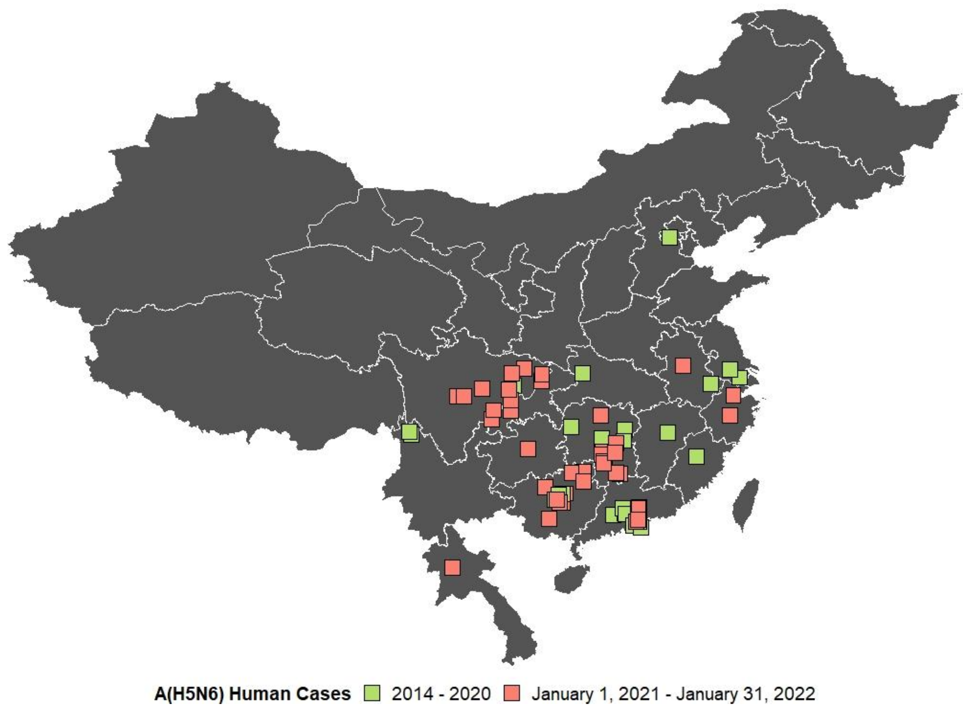
Variable	Sex		Age Group	
	Males (n=33)	*Females (n=33)*	*Children (<18 years old) (n=9)*	*Adults (≥18 years old) (n=57)*
Median Age (range)	53 (3-75)	47 (1-81)	4 (1-11)	52 (22-81)
Proportion Males (%)	N/A	N/A	22	54
Proportion Hospitalized (%)	97	91	56	100
Hospitalization Delay (Days)	3	3.5	3	3
Case Fatality Rate (CFR) (%)	67	59	38	69

Note: 29 males, 32 females, 9 children, and 52 adults had available hospitalization data, with 28 males, 29 females, 5 children, and 52 adults reporting history of hospitalization. Hospitalization delay refers to the median number of days from symptom onset to hospitalization, for hospitalized cases that also had available symptom onset and hospitalization date data (23 males, 26 females, 4 children, and 45 adults). Fifteen males, 22 females, 8 children, and 29 adults had final outcome data that were used to determine CFRs. Missing outcome information may affect the CFR of reported groups. This table contains data on cases reported from 2014 to January 31, 2022.

Geographic Distribution

Approximately 98% (65/66) of human avian influenza A(H5N6) infections have been reported from China. One (1) case was reported from a bordering country, Lao PDR, in March 2021. Within China, the cases to date have been detected in 14 different regions: Hunan Province (14 cases), Guangdong Province (13 cases), Guangxi Zhuang Autonomous Region (12 cases), Sichuan Province (10 cases), Chongqing Municipality (3 cases), Anhui Province (2 cases), Jiangsu Province (2 cases), Yunnan Province (2 cases), Beijing Municipality (1 case), Guizhou Province (1 case), Hubei Province (1 case), Jiangxi Province (1 case), Fujian Province (1 case), and Zhejiang Province (2 cases) [Figure 5].

Figure 5. Spatial distribution of human cases of avian influenza A(H5N6) in China and Lao PDR, 2014-January 31, 2022.



Note: The cases included in this figure are cases reported up until January 31, 2022. Source: CIRID's IMAT.

The majority of these cases have been reported in south or southeast China, coinciding with a high density and popularity of LBMs coupled with free-range farming practices in this region, as well as an abundance of water resources that serve as habitats for AIV hosts (30). However, one (1) case was reported in northern China for the first time in 2019 [Figure 6] (20). This case, a 59-year-old female, developed illness after cooking poultry (20). One (1) case from Lao PDR was detected in a child from Luang Prabang Province, who also reported history of poultry exposure.

Figure 6. Geographic spread of human cases of avian influenza A(H5N6) in China by year of illness onset or report date, 2014-January 31, 2022.

	Provincial Level Division	2014	2015	2016	2017	2018	2019	2020	2021	2022
North	Beijing						1			
South	Hunan	1		3				1	9	
	Guangdong	1	3	3		1			5	
	Guangxi			1		2			9	
	Sichuan	1							8	1
	Chongqing							1	2	
	Anhui			1				1		
	Jiangsu					1		1		
	Yunnan		2							
	Zhejiang								1	1
	Fujian				1					
	Guizhou							1		
	Hubei			1						
	Jiangxi		1							

No. of cases
1
2
3+

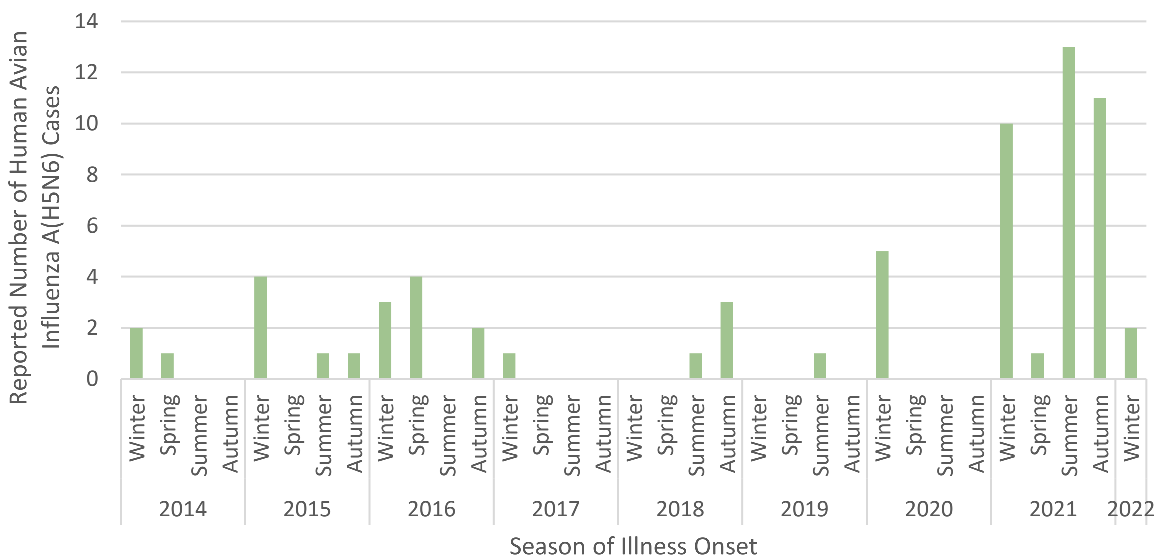
Note: Illness onset data were unavailable for three (3) cases; for these cases, report date was used to create this figure. The cases included in this figure are cases reported up until January 31, 2022. Source: CIRID's IMAT.

Timeline of Detections
The first report of human A(H5N6) infection was made on May 5, 2014, when China reported one (1) fatal A(H5N6) case in a poultry dealer from Sichuan Province. However, researchers retrospectively identified an A(H5N6) infection in a child who developed symptoms in February 2014, making her the first known human A(H5N6) case (32). This case was identified in Hunan Province, the region that has reported the highest number of cases (14/66; 21%) [Figure 6].

A marked increase in case incidence occurred in 2021, with nearly half of all cases (32/66; 48%) reported during this year [Figure 1]. Thirty-five cases (35/66; 53%) had symptom onset in 2021. These cases were reported from six (6) different regions in China [Figure 5] and A(H5N6) infected a resident in a different country (Lao PDR) for the first time, exhibiting greater geographic distribution than previous years. However, similar to prior cases, the cases with illness onset in 2021 had a median age of 54 years (age range: 3-75) and a comparable sex distribution (21/35; 60% males). Outcome data were available for 13 of the cases from 2021, of which ten (10/13; 77%) died. Human cases of A(H5N6) continue to be reported into 2022, with two (2) cases with illness onset in January 2022 notified as of January 31, 2022.

Although it has been postulated that an increase in cases may be observed in the winter and autumn, coinciding with influenza A seasonality in humans and avian migratory pathways, no seasonality was observed in the cases reported to date [Figure 7] (17). Cases are detected throughout the course of the year with a slight decrease in illnesses in the spring.

Figure 7. Epidemiologic curve of human avian influenza A(H5N6) infections, by season of illness onset or report date, 2014-January 31, 2022 (n=66).



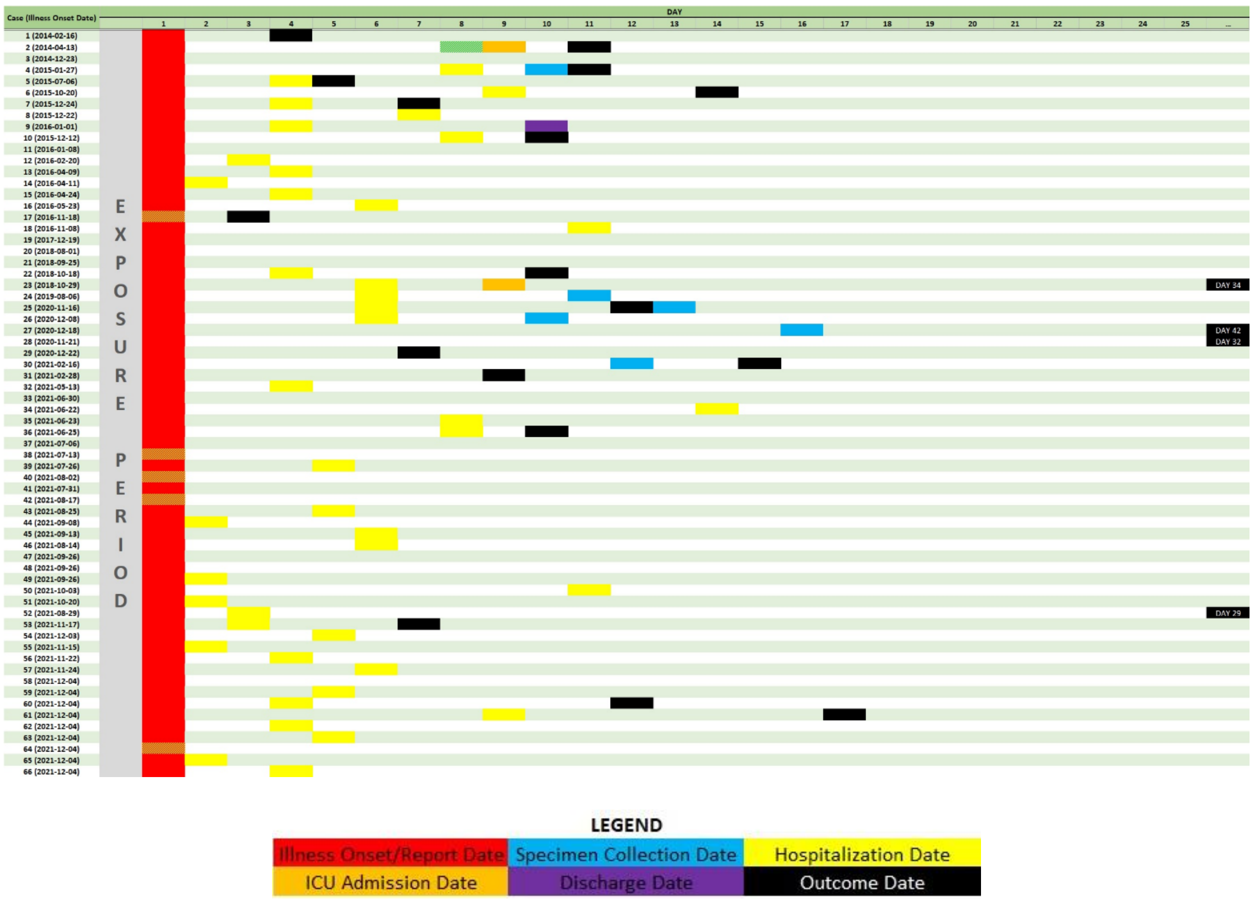
Note: Illness onset data were unavailable for three (3) cases; for these cases, report date data were utilized to create this figure. Winter includes the months of December, January, and February; spring includes March, April, and May; summer includes June, July, and August; and autumn includes September, October, and November. The cases included in this figure are cases reported up until January 31, 2022 so Winter 2022 only includes data from one month (January 2022) instead of three (3). Source: CIRID's IMAT.

CLINICAL COURSE

Signs and Symptoms

Similar to other human infections with HPAI H5 viruses, the clinical manifestation of human cases of avian influenza A(H5N6) often begins with fever, upper respiratory tract symptoms, and myalgia. This manifestation rapidly progresses to lower respiratory tract illness, resulting in pneumonia, multiple organ failure, acute respiratory distress syndrome (ARDS), and oftentimes death (33). The diagram below [Figure 8] outlines the clinical course of cases detected to date.

Figure 8. Clinical course of human avian influenza A(H5N6) infections, 2014-January 31, 2022 (n=66).



Note: illness onset data were unavailable for three (3) cases; for these cases, report date data were utilized to determine Day 1 of case clinical course. Hospitalization, ICU admission, discharge, and outcome (death or survival) dates were unavailable for several cases (26). Source: CIRID's IMAT.

Disease Severity

The case fatality rate (CFR) for human infections with A(H5N6) to date is 44% (29/66). Among the 61 cases with available hospitalization data, 93% (57/61) required hospital admittance, further highlighting the severity of this disease. However, this percentage should be interpreted with caution given data can be subject to selection bias. It is possible that cases are tested more often when they are severe and/or hospitalized, leading to a higher proportion of hospitalizations since the denominator might not capture most mild or asymptomatic cases. Conversely, it is also possible that there is undercounting of community deaths, e.g., where people do not present to hospital at all and are not tested for avian influenza infections. Research suggests mild or asymptomatic illness is uncommon with A(H5N6) and less likely as compared with other AIVs (30). Intensive care unit (ICU) admission details were too sparse to draw conclusions.

Outcome data were only available for 56% of the cases (37/66). Of these individuals, 38% (14/37) survived their infection, while 62% (23/37) died. When comparing details of fatal cases to non-fatal cases, fatal cases were older, had a higher proportion of hospitalized cases, and had a greater delay in hospitalization [Table 2]. Researchers propose longer delays in antiviral administration may also contribute to increased mortality, and have emphasized the importance of timely influenza testing, antiviral treatment, and increased healthcare professional awareness to mitigate negative outcomes (25). Of the fatal cases with known comorbidity information, half (3/6; 50%) reported the presence of comorbidities, as opposed to one-third (1/3; 33%) of the non-fatal cases. No large difference was observed in the male to female ratio of fatal and non-fatal cases [Table 2].

Table 2. Clinical outcomes of laboratory-confirmed human cases of avian influenza A(H5N6), 2014-January 31, 2022 (n=37)

Outcome of Illness	Number of Cases	Median Age (Age Range)	Male:Female Ratio	Proportion Hospitalized (%)	Median Time between Symptom Onset to Hospitalization (Days)
Alive	14	30.5 (1-65)	1:1.8	71	3
Deceased	23	49 (3-81)	1:1.3	100	5

Note: 20/23 (87%) fatal cases and 7/14 (50%) non-fatal cases had available symptom onset and hospitalization date data. One (1) non-fatal case that had missing symptom onset data but available hospitalization data had available report date data. The median time from symptom onset to hospitalization (days) was calculated for these 20 fatal and 8 (7 with symptom onset date data; 1 with report date data) non-fatal cases. The cases included in this figure are cases reported up until January 31, 2022. Source: CIRID's IMAT.

Since the earliest human A(H5N6) cases were detected in 2014, no data are yet available on the long-term clinical effects of A(H5N6) infection in humans.

PUBLIC HEALTH ACTIONS

Therapeutics and Vaccines

Antiviral administration may also help treat human cases of A(H5N6), but researchers have emphasized that antivirals be administered in a timely manner to reduce adverse outcomes (25).

The WHO coordinates the preparation of candidate vaccine viruses (CVVs) that may be used by vaccine manufacturers to produce influenza vaccines. As part of the global strategy for pandemic preparedness, the WHO has selected A(H5N6) clade 2.3.4.4 virus for development as a CVV. Two A(H5N6) clade 2.3.4.4 CVVs have already been developed (2.3.4.4e A/duck/Hyogo/1/2016 and 2.3.4.4a A/Sichuan/26221/2014) and five (5) others are pending (34) (6). However, considering the ever-changing genetic profile of HPAI A(H5N6), it is important to update CVVs frequently (19).

Public Health Measures

Adhering to public health measures like regular thorough handwashing, staying home if you feel sick, and minimizing contact with wild, sick, and/or dead birds and contaminated and/or high-risk environments (e.g. LBMs) may protect you and others from A(H5N6) infection. The WHO recommends avoiding contact with high-risk environments like LPMs or contaminated surfaces (26). For those who cannot avoid contacting birds, e.g. poultry farmers or others with occupational exposure, the use of personal protective equipment (PPE) may help prevent influenza infection (35). During outbreaks or following exposure to infected birds, research also shows biosecurity measures like antiviral prophylaxis could prevent infections (35). Seasonal influenza vaccination may also help prevent co-infections of novel and seasonal influenza, thereby reducing the risk of reassortants.

At a national level, Canada has engaged in several pandemic preparedness activities that mitigate the likelihood and impact of novel influenza [e.g. A(H5N6)] infections in humans. For instance, PHAC has issued planning guidance for the health sector in the case of an influenza pandemic. PHAC can also employ its National Emergency Strategic Stockpile (NESS), which contains supplies like medical equipment and pharmaceuticals to provide provincial and/or territorial regions relief and support in the event of emergencies like influenza outbreaks.

Surveillance
In addition to the public health measures outlined above, global surveillance is recommended by the WHO to detect virological, epidemiological, and clinical changes associated with viruses like A(H5N6) that can affect human and animal health. As AIV A(H5N6) continues to circulate in bird populations and contaminate various environments, more detections of sporadic human cases of A(H5N6) are expected. Timely information sharing of these cases under the International Health Regulations (2005) remains key for human A(H5N6) infection risk assessment and mitigation (26).

LINKS AND RESOURCES

- PHAC's FluWatch surveillance
- PHAC's Avian Influenza Travel Health Notice
- PHAC's National Emergency Strategic Stockpile
- PHAC's Protocol for Microbiological Investigations of Severe Acute Respiratory Infections (SARI)
- PHAC's SARI Case Definition
- PHAC's SARI Case Report Form
- PHAC's biosecurity guidance for H5/H7/H9 influenzas
- PHAC's surveillance guidance for avian influenza (specifically H7N9, but applicable to other HPAI like H5N6) in humans
- PHAC's CPIP: Planning Guidance for the Health Sector
- PHAC's Avian Influenza (Bird Flu)
- Canadian Food Inspection Agency (CFIA)'s Avian Influenza (bird flu)
- US CDC's Information on Avian Influenza
- North American Plan for Animal and Pandemic Influenza (NAPAPI)
- OIE's Avian Influenza
- Food and Agriculture Organization of the United Nations (FAO)'s Avian Influenza
- WHO's Surveillance – Avian influenza
- WHO's Risk assessment summaries of influenza at the human-animal interface

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