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Avian influenza A(H5N1) and the continuing outbreak

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Key Messages

- The outbreak of high pathogenicity avian influenza (HPAI) caused by A(H5N1) that began in late 2021 has persisted through to 2023, and has shown unprecedented spread through wild birds, poultry, and mammals in Canada and internationally.
- Few human infections have occurred in the current outbreak, and none in Canada; however, there is a need for continued vigilance to prevent opportunities for spillover to humans.
- The current outbreak of the circulating H5N1 clade 2.3.4.4b is an environmental health concern as it is very persistent, it is not following typical seasonal trends, and it has adapted to infection in mammals, including domestic pets.
- There is a risk that the virus could become endemic in the Americas, presenting challenges for managing continuing risks to poultry and wildlife in Canada, and increasing the potential for spillover to humans.
- Managing the ongoing outbreak and future risks requires continued surveillance of the global situation, and strengthened partnerships and coordination with, and beyond, the animal health sector using a One Health approach.
- Environmental public health practice has an important role to play in delivering on a One Health approach by:
    - leading on risk communication to the public and high-risk groups;
    - identifying important environmental drivers of transmission;
    - providing advice on preventing infection;
    - assisting in surveillance and outbreak investigations, especially for unusual hosts such as urban wildlife or domestic pets.

Introduction

In late 2021, a strain of highly pathogenic avian influenza (HPAI), commonly referred to as bird flu, began spreading among wild and farmed birds globally.[1] The outbreak, caused by influenza A(H5N1) persisted through 2022 and into 2023, and has resulted in deaths of wild birds and culling of millions of poultry birds across Canada over the past two years. Spillover into wild mammals was observed in North America for the first time in May 2022, and an increasing diversity of wild birds and mammals and a small number of domestic pets have since been affected. While the risk to humans remains low, the persistence of the current outbreak, the spread among a wide range of bird and mammal species, and threat of the virus

becoming endemic in the Americas warrants a fresh look at the current situation, including the types of measures a One Health approach encompasses to mitigate the impacts of the outbreak.

Methodology

This evidence brief provides an update on the A(H5N1) outbreak, covered in our previous May 2022 brief.[1] We searched recent (past 12 months) scholarly publications, grey literature, public agency websites, and media sources for emerging evidence on avian influenza A(H5N1) transmission patterns and updates to public health guidance or outbreak management approaches in Canada. Forward and backward chaining of key resources was used to identify additional resources. The findings were synthesized narratively and the synthesis was subjected to internal review.

Background

Avian influenza is a generic term referring to zoonotic type A influenza viruses that can infect a range of bird species.[2] Wild waterfowl are the major source of influenza A viruses, which can spillover to other species.[3] Various strains are referred to as A(H*x*N*y*) depending on the combination of specific antigens present on the viral surface, primarily hemagglutinin (18 subtypes H1-H18), and neuraminidase (11 known subtypes N1-N11).[4] Avian influenza A viruses can be categorized based on their levels of pathogenicity to birds — either low pathogenicity avian influenza (LPAI) or **high pathogenicity avian influenza (HPAI)**. These designations do not correlate with pathogenicity or severity of illness in humans. Some influenza A(H5) and A(H7) viruses are HPAI viruses and can easily transmit between different bird species, with a very high mortality rate.[5]

Globally, sporadic outbreaks of different avian influenza viruses have occurred in most years over the past two decades. The current outbreak is associated with influenza A(H5N1) and is considered to be HPAI. Outbreaks typically follow seasonal trends, with cases predicted to peak in February and decline to low levels in September.[6] Transmission is usually restricted to birds; however, infection of mammals and humans can occur. The first case of human infection with A(H5N1) was reported in Hong Kong in 1997 in an outbreak that resulted in 18 human infections and six deaths.[7] Since 1997, 892 confirmed human A(H5N1) infections and 464 deaths have been reported to the World Health Organization (WHO), with most infections and fatalities occurring prior to 2020.[8,9] One of the most significant outbreaks was in Egypt in 2014–15, where 169 human infections and 51 deaths occurred.[10] Only one human case of A(H5N1) has ever been detected in Canada, which resulted in a death in 2014 of an individual who had become infected while outside of Canada. The first occurrence of A(H5N1) in North American birds was

detected in December 2014 in a wild bird, followed by a widespread outbreak with significant losses to the poultry industry.[11] Subsequently, there were few detections in North America until 2021.

Overview of the current outbreak

The current outbreak in Canada was first detected in December 2021 with a new introduction of A(H5N1), clade 2.3.4.4b in farmed poultry that had been infected by migratory birds arriving on the Atlantic coast.[12] This clade originated in China around 2010–11 and has been shown to "reassort" with other avian influenza viruses, a process whereby gene segments are swapped between viruses to make a new genetic sequence when a host is infected with multiple influenza viruses.[13]

There have been changes in the transmission dynamics of the current A(H5N1) outbreak in the Americas, with symptomatic infections circulating in a much wider range of wild birds and mammals, and a departure from the typical seasonal patterns of infection.[14] The reassortment of an A(H5N1) clade 2.3.4.4b virus with a North American wild bird influenza virus soon after introduction in 2021 may be responsible for the emergence of a strain that is better adapted to infect a wider range of birds and mammals.[15] The outbreak has since spread across North, Central, and South America. Ongoing and recurring events have been observed in Europe, Asia, the Americas, and Africa throughout the first half of 2023,[6] in the most widespread and persistent outbreak of HPAI ever seen.[14]

Transmission to animals and humans

This section summarizes current reports on infections among wildlife, poultry, and humans and how the virus transmits to hosts (Boxes 1–4).

Wild birds

Over 2,000 detections of HPAI in wild birds have been reported in Canada since late 2021 via the Canadian wildlife surveillance dashboard, which reports cases detected via passive surveillance of sick or dead birds.[16] Total mortalities are likely much higher as not all sick or dead wild birds are collected or sent for testing, and many go undetected in nature. Water fowl and migratory birds are among the most affected species but terrestrial and non-migratory birds have also been widely impacted. About 90 species have been affected in Canada, with just six accounting for over half of the cases (Canada goose, American crow, snow goose, great horned owl, bald eagle, and mallard duck).

The virus presents a risk to endangered or vulnerable wild bird populations. In early 2023, twenty endangered California condors died due to A(H5N1) infection.[17] Vaccination of condors against HPAI has been approved in the US, and will begin with captive individuals before inoculation of wild birds.[18] In Peru, thousands of the near-threatened Peruvian pelicans have died due to the virus, and in Chile, over 2000 vulnerable Humboldt penguins have died, over 10% of the national population.[19-21] Other wild bird species that have had no prior exposure to the virus have also been impacted.

Box 1. How does the virus transmit among wild birds?

- Direct contact with other infected birds or surfaces, water, food, or soil contaminated with their feces or saliva,[22] especially in watering or nesting areas with a high concentration of infected birds.[23]
- Ingestion of contaminated meat (e.g., by raptors) while scavenging on carcasses of infected wildlife.
- Some birds diffuse more virus into the local environment and are a larger driver of spread (e.g., gulls, geese, swans).[23]
- Spillover from wild to domestic birds occurs more frequently than the reverse, but dispersal among similar groups (e.g., wild-to-wild or domestic-to-domestic) is most efficient.[23]

Poultry

Cases of HPAI have been reported by the Canadian Food Inspection Agency (CFIA) in both commercial poultry and backyard flocks in most provinces since 2021. Over seven and a half million commercial poultry and egg-producing birds have been culled across Canada as of July 2023.[24] Farms in BC account for almost half of the culled birds, most of which are located in the Fraser Valley. Over the winter of 2022–23, fewer premises were affected as wild birds migrated south, resulting in primary control zone orders being revoked in many parts of the country. However, in Spring 2023, new controls orders were implemented in some parts of Canada, with active orders still in place in BC, Alberta, and Quebec as of July 2023.[24] This suggests persistence of the virus among wild populations, and a need for continued vigilance among poultry and egg farmers.

Box 2. How does the virus transmit among poultry?

- Direct contact with infected wild birds, or surfaces, water, food, soil, or bedding contaminated with their feces or saliva.[3]
- Transmission among an infected flock via respiratory transmission, oral-oral transmission via shared drinking water sources, or fecal-oral transmission via water, food, or bedding.[22]
- Unintentional spread by farm workers or visitors via clothing, footwear, equipment, or vehicles.[25,26]
- Drinking water contamination at poultry premises is an important source of infection, and the virus can persist in water for days to weeks.[25,27,28]
- Ducks spread virus more efficiently than chickens or turkeys due to higher rates of infection and viral shedding.[25,26]

Mammals

Interspecies transmission from birds to mammals is rare[29]; however, the current outbreak has led to unprecedented spread among wild mammals in the Americas.[30] The Canadian wildlife surveillance dashboard has reported over 140 detections of confirmed or suspected HPAI in wild mammals in 2022–23. Most of these are attributed to just three species: striped skunk, red fox, and harbour seal. HPAI was also detected in raccoon, black bear, mink, dolphin, fisher, porpoise, and otter. Infected urban wildlife, such as skunks are a concern due to greater potential for interactions with domestic pets or humans. Most detections among mammals to date have been in Alberta, Ontario, Quebec, PEI, and BC. All of the marine mammal detections occurred in Quebec.

Infections in terrestrial and marine mammals have been reported elsewhere in the Americas. The US Department of Agriculture has detected HPAI in skunks, raccoons, foxes, coyotes, mountain lions, bears, opossum, dolphins, and seals. In South America, there have been significant deaths of marine animals, with Chile reporting over 13,000 dead sea lions in the current outbreak.[21]

A few cases of HPAI have been reported in domestic pets in North America and Europe. In April 2023, a domestic dog in Ontario that had chewed on a dead wild goose tested positive for A(H5N1) infection and later died.[31] In July 2023, a cluster of five dogs and one cat tested positive for H5N1 on an Italian poultry farm with an ongoing outbreak of HPAI.[32] In the US states of Oregon, Nebraska, and Wyoming, HPAI cases have occurred among pet cats, suspected to have occurred via contact with backyard chickens or predation of wild birds. In late June 2023, there were several reports of H5N1 infections in cats from

disperse geographical locations in Poland,[33] with 24 confirmed cases as of July 5th.[32] Since the cases were unrelated, and some of the cats did not have outside access, sources of possible exposure, including ingestion of raw poultry meat, are being investigated.

Box 3. How does the virus transmit among mammals?

- Direct contact with infected birds, including via ingestion of raw meat scavenged from infected carcasses.[14]
- Exposure to contaminated environments, particularly for marine mammals exposed to waters where infected flocks of water fowl have been nesting or feeding.[34]
- Mammal-to-mammal transmission is rare, but cannot be ruled out where there have been large outbreaks (e.g, farmed mink in Spain, sea lions in South America, seals in the US).[34,35]

The current strain appears to cause severe disease and death in some infected mammals, including high viral load in the brain and severe neurological symptoms.[15] However, experimental inoculation of mammals such as pigs demonstrated a high level of resistance to clade 2.3.4.4b infection.[36]

Humans

Human infection with influenza A(H5N1) is very rare,[37] but risks are higher for persons who have close and prolonged contact with infected birds or contaminated environments (e.g., poultry workers).[3,38,39] Between 2021 and July 2023, there were 14 human cases of A(H5N1) detected globally, with two cases in 2021 (India and UK), six cases in 2022 (China, Ecuador, Spain, US, Vietnam), and six cases in 2023 to date (Cambodia, Chile, China, UK). Three deaths have occurred.

Most of the cases to date belong to clade 2.3.4.4b except for the cases in Cambodia, including one fatality, which were clade 2.3.2.1c. Most cases with severe or fatal outcomes in the current outbreak were exposed to sick or dead backyard poultry and were not wearing personal protective equipment (PPE). A case from Chile of a 53-year-old man, who required hospitalization in intensive care, had no known source. Infection may have resulted from environmental exposure. The man lived near a beach area where a mass die-off of sea lions and wild birds due to HPAI had occurred, and there were birds detected near, and in, a building he used as a workshop.[40]

Two asymptomatic cases were detected in May 2023 as part of the UK Health Security Agency asymptomatic testing programme of poultry workers working on infected farms.[9,41] Among these, and

other asymptomatic cases reported in poultry workers since the beginning of the outbreak (Spain, UK, and US), there is speculation that positive test results may have been due to contamination of the nasal mucosa or throat with ambient virus, rather than infection. In the cases in Spain in 2022, serological testing found no antibodies for H5.[42] These workers did not show signs of symptomatic infection, and no onward transmission to close contacts was detected.

To date, human infections have not resulted in sustained onward transmission to others. Human-to-human transmission has previously occurred in a healthcare setting following prolonged, close, and unprotected contact with a severely ill patient.[7] In some small familial clusters, human-to-human transmission may have occurred, but infection may also have been caused by a common exposure to sick birds or contaminated environments, such as exposure to infected bird feces in garden fertilizer, or bathing in small lakes or canals where infected birds were present.[27,39,43]

Consumption of cooked poultry, game meat, or eggs has not been found to be a route of transmission, although the virus can persist in raw meat and on egg surfaces, or in uncooked egg albumin and yolks. A(H5N1) can be inactivated by cooking meat and eggs thoroughly.[44-46]

Box 4: How does the virus transmit to humans

- Direct contact with infected birds, manure, or contaminated surfaces, equipment, clothing or footwear via inhalation, or direct conjunctival, intranasal, or oral contact.[39]
- H5N1 infection occurs via binding to receptors in the respiratory tract, but HPAI viruses do not replicate well in upper respiratory tract of humans, limiting human-to-human transmission.[7,47]

Managing the outbreak going forward

While there have been few human infections or deaths in the current outbreak, there have been significant deaths among wildlife and poultry, economic impacts on the poultry industry from culling of animals, restrictions on trade, and job losses, and added pressures on food security as some poultry and egg products become more unaffordable. There is a risk of further endangerment or eradication of wild species, which in turn could threaten global biodiversity and health security.[48] Recent mass mortality among seabird colonies, including gulls, in Europe increases the likelihood of human exposures to sick or

dead birds. The European Centres for Disease Control and Prevention (ECDC) thus published guidance on enhanced surveillance of avian influenza infection in hospital settings in June 2023.[49]

The persistence of the virus in wildlife and recurrence of outbreaks globally, presents additional risks during the migratory bird season in North America later in 2023. There are concerns that the virus could become endemic in the Americas, and further human cases are possible.[50] The risk of infection for humans could change as a result of reassortment events or genetic mutations that cause greater adaptation to infections in mammals, increasing the potential for further spillover.[3,14,15,35,51] Reassortment to a more transmissible strain could also occur if a human has a concurrent infection with A(H5N1) and a human influenza virus.[13]

These issues underscore the interconnectedness of animals and the environment with global human health issues and the need to manage HPAI risks using a **One Health approach** that addresses the multiple drivers of transmission.[14,48] One Health is an approach to managing emerging health threats by recognizing the interdependencies of human, animal, and environmental health.[52] It requires multi-sectoral partnership and coordination to enable early detection among farmed animals, wildlife, and humans, and to set priorities for response to prevent further spread and spillover. This requires good communication across groups and geographies, information and data sharing, and awareness raising and education among groups that could be exposed or can help reduce spread. Many groups have a role including:

- Federal agencies, such as CFIA, Environment and Climate Change Canada (ECCC), Health Canada (HC), and the Public Health Agency of Canada (PHAC);
- Provincial and territorial ministries (e.g., agriculture, forestry, environment) and public health units;
- Academic institutions and interagency partnerships, such as the Canadian Wildlife Cooperative;
- Industry groups (agriculture, food, wildlife tourism);
- Special interest groups such as wildlife NGOs, and citizen science groups;
- Indigenous communities, Guardians, and knowledge keepers;
- Occupational health and safety organizations;
- Clinicians.

Some of the key considerations for managing the outbreak across the animal, environmental, and human health domains encompassed by a One Health Approach are discussed below.

Animal health considerations

The CFIA takes a leading role in animal health responses, establishing quarantines, ordering culling of infected flocks, contact tracing, and overseeing biosecurity measures in the poultry sector. Surveillance is essential to early identification of sick birds to prevent onward transmission. Biosecurity measures on

poultry farms may need to be heightened in areas where wildlife or poultry flocks have been found to be infected. Culling is one of the primary prevention tools to stop spread between flocks and farms within a region but comes at a large cost. Preventive biosecurity measures can reduce transmission, and the CFIA's National Avian On-Farm Biosecurity Standard provides detailed advice to owners or managers of poultry production facilities and people who handle or keep poultry, from large-scale producers to backyard and domestic bird keepers.[53] Regional or farm-scale measures could include designation of control zones, or reducing density of commercial establishments or housed birds to prevent spillover between farms. Measures to protect flocks from exposure to wild birds or mechanical vectors (e.g., rodents or insects that inadvertently transport viral particles externally) could include keeping birds indoors and establishing barriers to wildlife interacting with flocks.[54] Personnel can take measures to prevent cross contamination between poultry houses or farms by using PPE and being aware of transmission risks from contaminated clothing, footwear, equipment, or vehicles.[44] Culled birds also need to be carefully disposed of to reduce risks of transmission from carcasses.[46,53]

Vaccinating poultry has been considered as a preventive measure in some countries or regions where there is a high risk of transmission, or in an emergency to help control an outbreak in progress.[55] There are some concerns and barriers to the use of vaccination, such as trade barriers, costs, and logistics of a mass vaccination program,[55] and incomplete information on the effectiveness against asymptomatic infection. Vaccination does not remove the need for continued surveillance and biosecurity measures. The practice of vaccinating poultry against HPAI has previously been applied in China (H5 and H7) and was approved in Mexico in late 2022. More recently France has announced a programme of mass-vaccination of poultry against HPAI, beginning with ducks, due to start in September 2023.[56]

Environmental considerations

Wild birds, and increasingly wild mammals, are reservoirs of the virus; hence, wildlife surveillance is needed to understand viral evolution and persistence. Surveillance of HPAI in wildlife is usually passive, based on testing of carcasses of deceased birds or other wildlife reported to the Canadian Wildlife Health Cooperative (or the BC Wildlife Health Program).[16] Groups that are more likely to interact with wildlife (citizen science groups, outdoor professions, Indigenous communities) can be important to identifying and reporting wildlife that are sick or have died from unknown causes. There is limited active surveillance to detect the occurrence of asymptomatic or mild infections among wildlife.

Some environmental conditions or times of year may present greater transmission risks. For example, HPAI viruses are more persistent at low temperatures[27,57] and in waters of neutral to basic pH (7.0–8.5), low salinity (<0.5 ppt), and low ammonia concentration (<0.5 mg/liter).[58] Waterborne transmission is an important driver of infection in aquatic birds. Seasonally, bird migration can allow for resurgence of disease among wild bird populations due to increased density of birds and environmental contamination. Breeding sites or overwintering grounds can thus become hot spots for transmission, but are also popular

locations for wildlife viewing. In certain environments or at some times of the year, enhanced surveillance or awareness raising may be needed to quickly identify sick or dead birds, and to encourage vigilance among the public.

Biosecurity measures are difficult to deploy for wildlife, particularly for very mobile or marine species.[34] Some measures, such as carcass removal could help to prevent environmental contamination in areas of low bird density, and reduce opportunities for scavenging of infected carcasses by raptors, mammals, or pets. In a mass mortality event of wild birds, carcass removal may be less effective for reducing transmission to other wildlife, due to the widespread environmental contamination that has already occurred (e.g., in a seabird nesting site).[59] It could also cause some disruption to bird colonies causing increased movement of infected birds to new areas, or allow dissemination of virus within or beyond a site via footwear, clothing, or equipment of personnel collecting carcasses.

Habitat loss due to development, climate change, or natural disasters can cause increased density of wildlife in ever shrinking habitats, or cause wildlife to seek out alternative habitats or change migratory patterns and stopover areas.[60] Environmental degradation or pollution can also impact natural food sources, which can cause wildlife to seek out food sources closer to humans, in urban settings or agricultural sites, increasing the potential for spillover. Thus, preventing spread, and opportunities for spillover, may require longer-term solutions such as habitat restoration and environmental protection measures.

Human health considerations

Ensuring prevention of infection, early detection and reporting, contact tracing, genomic surveillance, and sharing of epidemiological investigations of cases in humans are a shared responsibility. Federal agencies (PHAC, HC, and ECCC) provide advice and resources on preventing HPAI transmission for the public (Box 5),[61-64] and occupational health and safety organizations provide advice specific to higher risk professions (e.g., poultry workers, conservation workers, parks personnel, veterinarians, researchers).[44,65]

Clinicians have a role in detecting occurrence of HPAI in patients with influenza symptoms who have had recent exposures to wildlife or poultry. Clinicians must report any infections of influenza A (H5N1) to the medical health officer, and public health is involved in essential follow-up activities. These include epidemiological investigations, detailed case reports, and genomic analysis, which are all essential to understanding patterns of transmission as well as the evolution of the virus to identify changes in pathogenicity to humans. Timely sharing of this information nationally and internationally can enhance preparedness and response activities globally.[49]

Currently there is no HPAI vaccine licensed for use in humans or animals in Canada, but seasonal influenza vaccination is recommended for persons at high risk of exposure to HPAI, to reduce the risks associated with a co-infection with HPAI and a human influenza virus.[66]

Box 5. General advice for members of the public[38,61-64,67,68]

- Avoid feeding or interacting with wild birds or handling feathers in areas of HPAI infections.
- Keep children and pets away from wild birds and their droppings.
- Report sick or dead wildlife to the Canadian Wildlife Health Cooperative (most of Canada) or to the BC Wild Bird Mortality Line in BC.
- Avoid handling or eating wild animals that appear to be sick or have died from unknown causes.
- For people who hunt or collect eggs in the wild:
  - Avoid collecting heavily soiled or cracked eggs, and do not wash eggs.
  - Avoid direct contact with blood, feces, and respiratory secretions of wild game and exposure to dust, feathers, or aerosols by working in a well-ventilated space or wearing a mask.
  - Avoid eating, drinking, smoking, or touching eyes or face while preparing wild game (wash hands before and after).
  - Thoroughly cook meat, organs, and eggs harvested from the wild to an internal temperature of 74°C for meat and eggs and 82°C for whole birds.
- Prevent pets from accessing sick or dead birds by keeping dogs on a leash and cats indoors, keeping food and water bowls inside and not feeding pets raw meat from potentially contaminated carcasses.
- Avoid feeding waterfowl and gulls, keeping backyard bird feeders or baths away from poultry and domestic animals, and cleaning feeders and baths regularly.[62]
- Remove backyard feeders during the summer months (April–September) to reduce congregation points for wild birds.[68]
- Reduce opportunities for backyard chickens to interact with wild birds or their droppings, check for signs of illness, keep sick birds away from others, and don't bring sick birds inside.

Environmental public health practice has an important role to play in surveillance and in public health protection, via communication of hazards and infection control precautions, such as measures identified in Box 5, as well as assisting in tracing outbreaks in animals, especially infections among unusual hosts such as domestic pets or urban wildlife.

Conclusions

The persistence of the current A(H5N1) outbreak has demonstrated an ability of the virus to reassort, evolve, and acquire additional mutations that has led to persistence of the virus and infection of a wider diversity of bird and mammal species than has ever been seen before. This increases the potential for spillover risk to humans and threatens global biodiversity, while also contributing to economic and food security impacts. Continued transmission of the virus among wild, commercial, and domestic birds and mammals could result in additional bird deaths, culling of infected flocks, and threats to wildlife conservation efforts.

Given these issues, multi-sectoral partnerships, cooperation, and information sharing are needed nationally, and internationally, to ensure a One Health approach to management and mitigation of the outbreak, encompassing wildlife, poultry, and human health measures. While animal health measures often take centre stage in managing avian influenza outbreaks, environmental public health professionals have an important role in ensuring the environmental drivers of transmission and human health risks are considered, and communicated, in order to prevent continued transmission or opportunities for spillover.

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