REVIEW ARTICLE

IDSA OXFORD

Avian Influenza Virus Infections in Felines: A Systematic Review of Two Decades of Literature

Kristen K. Coleman[1,2,] and **Ian G. Bemis**[1,2]

[1]Department of Global, Environmental, and Occupational Health, University of Maryland School of Public Health, College Park, Maryland, USA, and [2]Department of Veterinary Medicine, College of Agriculture and Natural Resources, University of Maryland, College Park, Maryland, USA

As an avian influenza virus (AIV) panzootic is underway, the threat of a human pandemic is emerging. Infections among mammalian species in frequent contact with humans should be closely monitored. One mammalian family, the Felidae, is of particular concern. Domestic cats are susceptible to AIV infection and provide a potential pathway for zoonotic spillover to humans. Here, we provide a systematic review of the scientific literature to describe the epidemiology and global distribution of AIV infections in felines reported from 2004 to 2024. We identified 607 AIV infections in felines, including 302 associated deaths, comprising 18 countries and 12 felid species. We observed a drastic flux in the number of AIV infections among domestic cats in 2023 and 2024, commensurate with the emergence of H5N1 clade 2.3.4.4b. We estimate that this phenomenon is underreported in the scientific literature and argue that increased surveillance among domestic cats is urgently needed.

Keywords. avian influenza virus; cats; felines; One Health; zoonosis.

Avian influenza virus (AIV) is an important and emerging zoonotic and reverse-zoonotic viral pathogen with pandemic potential. AIV has caused substantial disruptions to food supply chains, resulting in large economic losses in the poultry industry, as well as disruptions to regional and global food security. As avian influenza has a high mortality rate, an AIV pandemic could result in substantially more human illnesses and deaths than recent pandemics. While current surveillance is focused on AIV as an emerging pathogen in US dairy cattle, infections among other susceptible domestic mammalian species have received comparatively little attention. In particular, AIV infections in free-roaming and farm-associated domestic cats are rising in the United States [1, 2], but overall surveillance efforts among felines appear sparse.

Domestic cats are a popular human companion animal and thus provide a potential pathway for zoonotic spillover of avian influenza viruses to and from humans. Avian influenza in felines is often fatal, although subclinical infections have been reported [3, 4]. Felines prey on wild birds and mammals and may serve as a host for AIV adaptation to mammals. Feline-to-feline transmission of AIV has been demonstrated experimentally [5, 6], and real-world outbreaks among felines resulting in human infections have been reported [7–9]. To provide a comprehensive background for assessment of the current risk, as well as to bring awareness to the recurring phenomenon of AIV infection in felids, we performed a systematic review of AIV infections in felines reported in the peer-reviewed scientific literature from 2004 through 2024. In this review, we sought to characterize the epidemiology and global distribution of AIV infections in felid species of domestic and wild origin reported over time, including information on AIV subtypes and clades identified.

METHODS

Electronic Literature Search and Article Selection

We conducted systematic electronic searches for peer-reviewed articles in the English scientific literature to identify eligible studies. Our search strategy is presented in Supplementary Table 1. A study was eligible to be included if the following criteria were met: (1) avian influenza virus infection (including the abbreviation AIV) in "felines," "felids," or "cats" mentioned in the abstract, main text, or within keywords, including *Pantherinae* species names (ie, lion, tiger, jaguar, leopard, snow leopard) and *Felinae* species names (eg, cheetah, caracal, cat, wildcat, jaguarundi, ocelot, oncilla, tigrillo, kodkod, güiña, margay, southern tigrina, serval, lynx, bobcat, manul, cougar, puma, and catamount), and (2) surveillance/epidemiological studies, case reports, or laboratory/bioinformatics studies of animal samples (or data from animal samples) that report original/primary evidence of avian influenza virus detection in felines/cats within the abstract or main text. We excluded studies where

(1) sound detection methods for the identification of avian influenza virus were not used, (2) original/primary evidence of avian influenza virus detection was not reported (eg, genomic studies of avian influenza virus specimens already reported in the peer-reviewed literature), (3) only experimental infection studies were performed, and (4) publication was after December 2024. Note that genomic studies of previously collected avian influenza virus specimens were included if the specimens were not reported elsewhere in the peer-reviewed scientific literature. Studies selected for inclusion are listed in Table 1.

Data Extraction and Statistical Analysis

Data such as number of avian influenza virus infections, subtype, clade, location, intra- or cross-species transmission, disease characteristics, outcomes, and species infected were extracted from full-text articles using a data collection form. Data were imported to STATA, version 15.1 (StataCorp, College Station, TX, USA), for descriptive statistical analyses.

RESULTS

Our electronic search generated 207 articles through PubMed and 207 through Scopus. We identified a total of 18 experimental feline infection studies [5, 6, 52–67] and excluded them from our review. After further screening, we included a total of 48 articles in our review (Table 1), 2 of which were identified manually through article references [28, 33]. Of these articles, 33 used reverse transcription polymerase chain reaction (RT-PCR) alone or as a preparation for sequencing, and 13 used serology as their primary method of detection. See Figure 1 for a PRISMA consort diagram of article screening and selection.

Avian Influenza Virus Infections in Felines Reported Over Time

From 2004 to 2024, ~607 avian influenza virus infections in felines, including 302 associated feline deaths, were reported in the English scientific literature. In total, 184 of these infections were identified by serological methods alone, while the rest were identified by RT-PCR or viral culture followed by genome sequencing. A total of 62.6% (380/607) of the reported feline cases were domestic cats. The annual number of articles reporting avian influenza virus infections in felines drastically increased in 2023 (Figure 2), with a recent spike in the total number of domestic cat infections and deaths reported in 2023 and 2024 (Figures 3 and 4). This spike is commensurate with the emergence and increased spread of avian influenza virus H5N1 clade 2.3.4.4b among birds and mammals. As publication year may not be representative of the actual year(s) in which reported feline infections occurred, we provide data on the specific year(s) samples were collected (Table 1).

Avian Influenza Virus Subtypes, Clades, and Fatality Rates in Felines

The overall case fatality rate among the reported RT-PCR-confirmed feline infections identified in our review was estimated to be 71.3%. Among the avian influenza virus infections reported in felines, 92.3% were identified as highly pathogenic avian influenza (HPAI) and 7.7% as low pathogenic avian influenza (LPAI). Among the RT-PCR-positive feline infections, HPAI accounted for 99.7% of the deaths.

Among all RT-PCR-confirmed feline infections, 98% (414/422) were specifically identified as HPAI H5N1, which had an overall case fatality rate of 71%. Among the H5N1 cases, 33.8% (140/414) were identified as clade 2.3.4.4b, of which 96.4% (135/140) were domestic cats. Among domestic cats, the overall PCR-confirmed case fatality rate was 52.8% for H5N1 and 89.6% for H5N1 clade 2.3.4.4b. See Table 2 for the remaining avian influenza virus subtypes and clades, including their respective case fatality rates, reported in felines.

Influenza A H5N1 clade 2.3.4.4b was first detected in felines in 2022, including a wild lynx, during an outbreak among pheasants in Finland [36], and was detected in a domestic cat living near a duck farm in France [37]. All studies reporting feline infections occurring since that time have identified H5N1 clade 2.3.4.4b as the causative agent [1, 2, 4, 38–40, 42, 43, 45, 46, 49–51], aside from 2 serology studies that did not report the specific clade of the H5 virus identified [44, 48].

Among the publications that described the symptoms and pathology of the reported feline infections, respiratory and neurological illness were the most common and often resulted in death. Blindness and chorioretinitis were also recently observed in 2 AIV-infected domestic cats exposed to the virus through drinking raw colostrum and milk containing high viral loads from dairy cattle infected with H5N1 clade 2.3.4.4b [2]. This clinical observation suggests that exposure route and dose of AIV might impact disease presentation and severity. Although avian influenza in felines is often severe and fatal [6, 37], subclinical infections have been reported [3, 4].

Geographic Distribution of Avian Influenza Virus Infections in Felines

Infections among 10 felid species across 7 geographical regions of the world have been reported (Figure 5). The majority of reports (50%) were from Asia (including Southeast Asia), followed by Europe (25%) and North America (16.7%) (Supplementary Figure 1).

Feline infections of H5N1 clade 2.3.4.4b have been reported in Finland, France, Poland, the United States, Italy, Peru, and South Korea [1, 2, 4, 36–40, 42, 43, 45, 46, 49], including 5 species (135 domestic cats, 2 bobcats, 1 lynx, 1 caracal, and 1 lion). Zoos, animal shelters, and rural settings such as farms and private land were the most common settings where AIV infections in felines were reported to occur.

Cross- and Intraspecies Transmission of Avian Influenza Virus in Felines

Most of the reported AIV infections in felines were confirmed or suspected to be a result of bird-to-feline transmission. Eating dead pigeons, chickens, and other birds, as well as contaminated

Table 1. Publications Included in Our Systematic Review of Avian Influenza Virus Infections in Felines Published From 2004 to 2024, Including Country, Feline Species, Influenza Subtypes, Clades, and Year(s) of Study

Reference	Year Published	Country	Feline Species	Subtype(s)	Clade	Study Years
Keawcharoen et al. [10]	2004	Thailand	Tiger (*Panthera tigris*) & leopard (*P. pardus*)	H5N1	…	2003
Thanawongnuwech et al. [7]	2005	Thailand	Tiger (*P. tigris*)	H5N1	…	2004
No authors listed [11]	2006	Germany	Domestic cat (*Felis catus*)	H5N1	…	2006
Songserm et al. [12]	2006	Thailand	Domestic cat (*F. catus*)	H5N1	…	2004
Yingst et al. [13]	2006	Iraq	Domestic cat (*F. catus*)	H5N1	…	2006
Leschnik et al. [3]	2007	Austria	Domestic cat (*F. catus*)	H5N1	…	2006
Klopfleisch et al. [14]	2007	Germany	Domestic cat (*F. catus*)	H5N1	…	2006
Mushtaq et al. [15]	2008	China	Tiger (*P. tigris*)	H5N1	Clade 2.2	2005
Lam et al. [16]	2008	Indonesia	Domestic cat (*F. catus*)	H5N1	…	2005–2007
Desvaux et al. [17]	2009	Cambodia	Tiger (*P. tigris*), Asian golden cat (*Catopuma temminckii*), leopard (*P. pardus*), clouded leopard (*Neofelis nebulosa*)	H5N1	Clade 1	2004
El-Sayed et al. [18]	2013	Egypt	Domestic cat (*F. catus*)	H5N1	…	…
He et al. [19]	2015	China	Bengal tiger (*P. tigris tigris*)	H5N1	…	2013
Zhou et al. [20]	2015	China	Domestic cat (*F. catus*)	H5N1 and H9N2	…	2010–2012
Sun et al. [21]	2015	China	Domestic cat (*F. catus*)	H5N1	…	2013
Yu et al. [22]	2015	China	Domestic cat (*F. catus*)	H5N6	…	2014
Zhao et al. [23]	2015	China	Domestic cat (*F. catus*)	H5N1	Clade 2.3.2	…
Hu et al. [24]	2016	China	Tiger (*P. tigris*)	H5N1	2.3.4.4e, 2.3.2.1b, and 2.3.2.1c	2014 and 2015
Chen et al. [25]	2016	China	Lion (*P. leo*)	H5N1	Clade 2.3.2.1c	2016
Newbury et al. [26]	2017	USA	Domestic cat (*F. catus*)	H7N2	…	2016
Cao et al. [27]	2017	China	Domestic cat (*F. catus*)	H5N6	Novel reassortants	2016
Lee et al. [8]	2017	USA	Domestic cat (*F. catus*)	H7N2	…	2016
Mahardika et al. [28]	2018	Indonesia	Domestic cat (*F. catus*)	H5	…	2006
Kim et al. [29]	2018	Korea	Leopard cat (*Prionailurus bengalensis*)	H5	…	2011–2016
Wang et al. [30]	2018	China	Siberian tiger (*P. tigris altaica*)	H5 and H9	…	2015–2016
Lee et al. [31]	2018	South Korea	Domestic cat (*F. catus*)	H5N6	…	2016
Sangkachai et al. [32]	2019	Thailand	Bengal tiger (*P. tigris tigris*)	H5N1	…	2012 and 2013
Soilemetzidou et al. [33]	2020	Namibia	Caracal (*Caracal caracal*)	H1, H3, H5, H7, H8, H9, H11, H13, H14, and H16	…	2009–2013
Zhao et al. [34]	2021	China	Domestic cat (*F. catus*)	…	…	2017
Bao et al. [35]	2022	China	Domestic cat (*F. catus*)	H3N8	Reassortant	2022
Tammiranta et al. [36]	2023	Finland	Lynx (*Lynx lynx*)	H5N1	Clade 2.3.4.4b	2022
Briand et al. [37]	2023	France	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2022
Rabalski et al. [38]	2023	Poland	Domestic cat (*F. catus*) & caracal (*C. caracal*)	H5N1	Clade 2.3.4.4b	2023
Domańska-Blicharz et al. [39]	2023	Poland	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2023
Sillman et al. [1]	2023	USA	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2023
Moreno et al. [4]	2023	Italy	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2023
Szaluś-Jordanow et al. [40]	2023	Poland	Domestic cat (*F. catus*)	H5N1	…	2023
Yang et al. [41]	2023	China	Domestic cat (*F. catus*)	H9N2	Clade C1.2	2018
Elsmo et al. [42]	2023	USA	Bobcat (*Lynx rufus*)	H5N1	Clade 2.3.4.4b	2022
Cruz et al. [43]	2023	Peru	Lion (*P. leo*)	H5N1	Clade 2.3.4.4b	2023
Villanueva-Saz et al. [44]	2024	Spain	Domestic cat (*F. catus*)	H5	…	2022–2023
Lee et al. [45]	2024	South Korea	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2023
Kang et al. [46]	2024	South Korea	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2023
Burrough et al. [2]	2024	USA	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2024

Table 1. Continued

| Reference	Year Published	Country	Feline Species	Subtype(s)	Clade	Study Years
Cavicchio et al. [47]	2024	Italy	Domestic cat (*F. catus*)	H5	…	2021–2022
Duijvestijn et al. [48]	2024	Netherlands	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2020–2023
Caserta et al. [49]	2024	USA	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2024
Chothe et al. [50]	2024	USA	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2024
Mainenti et al. [51]	2024	USA	Domestic cat (*F. catus*)	H5N1	Clade 2.3.4.4b	2024
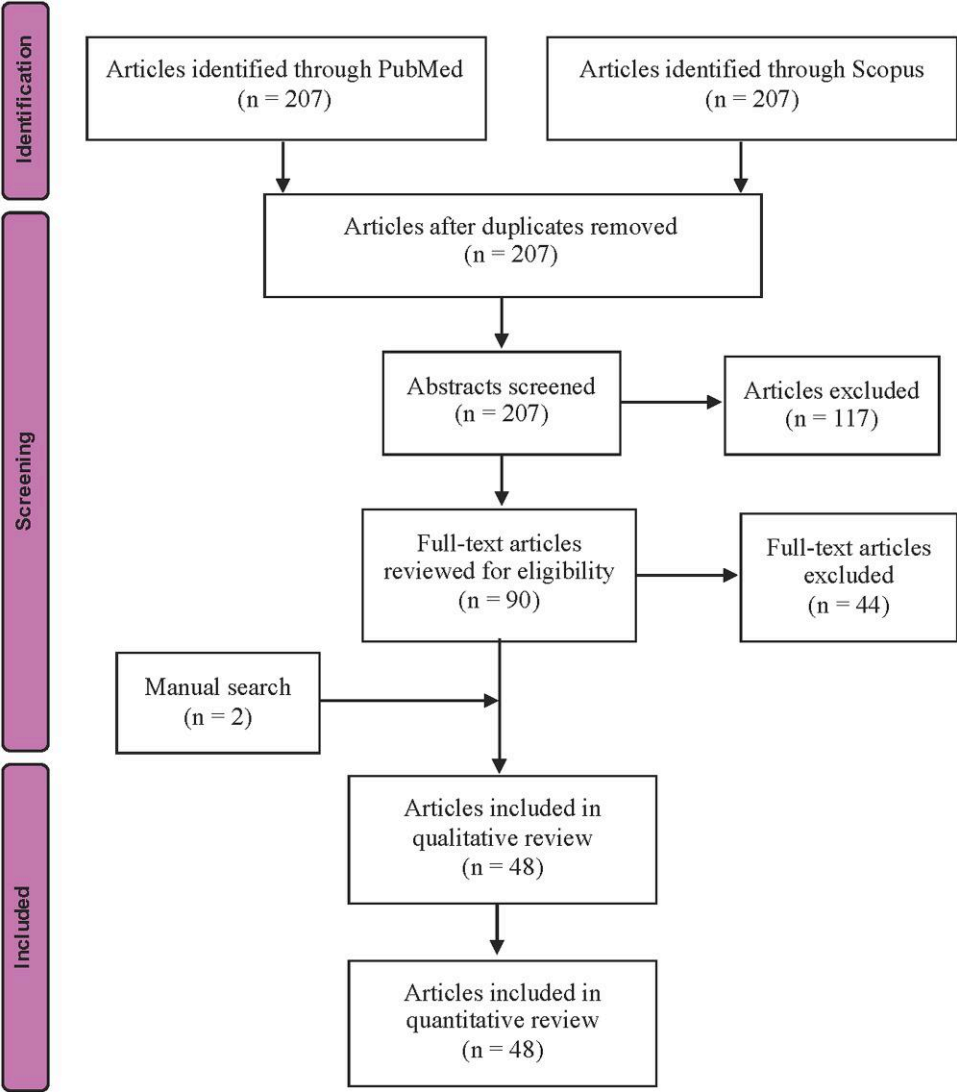
Figure 1. PRISMA flow diagram for identification, screening, and review of the peer-reviewed scientific literature on avian influenza virus infections in felines published from 2004 to 2024. Abbreviation: PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses. Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

raw chicken feed, was often implicated [6, 51]. Domestic farm cats fed raw colostrum and milk from AIV-infected dairy cattle in Texas have also been infected [2], demonstrating a new route of cross-species, mammal-to-mammal transmission. Two studies, not including experimental infections, reported probable intraspecies (feline-to-feline) transmission of AIV, including tiger-to-tiger [7] and domestic cat-to-cat [8] transmission. Feline-to-human transmission of AIV has also been documented [7–9]. The first study to report feline-to-human transmission involved an outbreak of H5N1 among captive tigers in Thailand,
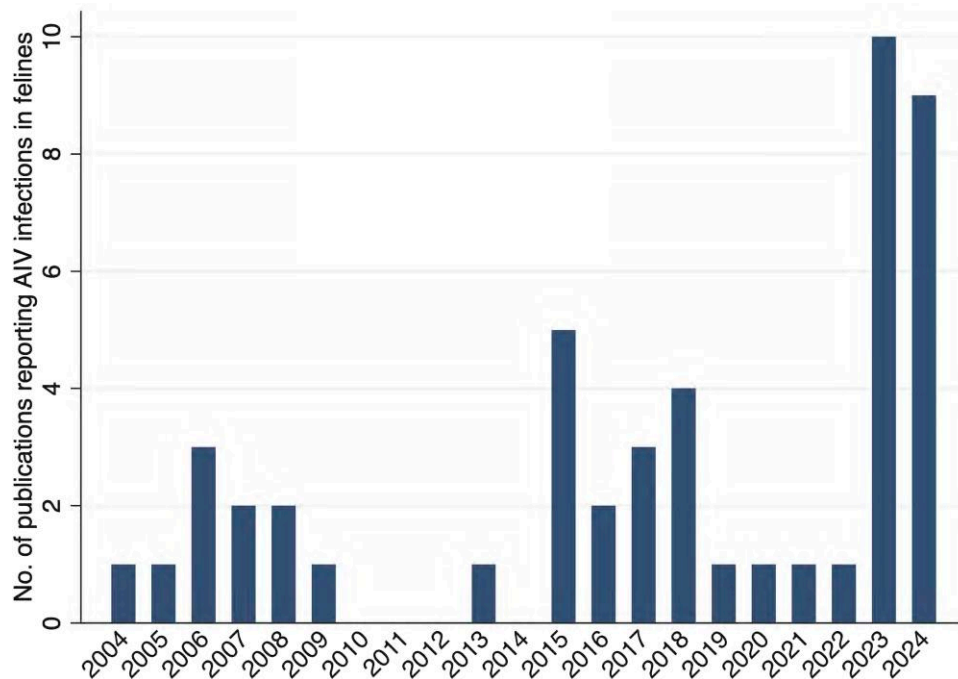
Figure 2. Number of peer-reviewed publications reporting avian influenza virus infections in felines each year from 2004 to 2024. Abbreviation: AIV, avian influenza virus.

after which 2 humans showed evidence of seroconversion [7]. The second involved a large outbreak of H7N2 among domestic cats in an animal shelter in New York, where 2 humans were infected, including a visiting veterinarian who collected samples from infected cats [8] and an animal shelter worker exposed to the infected cats [9]. Culture-positive air and surface samples were collected from the cat quarantine facility, demonstrating potential airborne and indirect-contact (fomite-mediated) transmission [68]. An experimental animal study [6] of this particular H7N2 strain reported that ∼500 cats were infected in animal shelters in New York, but we could not identify the primary source of this information.

DISCUSSION

Through our systematic review, we identified 607 avian influenza virus infections in felines, including 302 associated feline deaths, reported in the English scientific literature from 2004 to 2024. The reports represent cases from 7 geographical regions, including 18 countries and 12 felid species. The observed increase of AIV infections in felines over the past several years is commensurate with the rapid emergence of H5N1 clade 2.3.4.4b in other mammalian species. H5N1 clade 2.3.4.4b represents a variant in the hemagglutinin serotype 5 gene of IAV, which became the dominant IAV H5 serotype among poultry in 2020 [69]. Clade 2.3.4.4b is the causative agent responsible for the observed spike in AIV infections among domestic cats in 2023 and 2024, involving at least 7 countries.

To date, HPAI H5N1 has been identified in at least 26 wild mammalian species in the United States [70]. As with many zoonotic pathogens, morbidity and mortality from AIV differ by species and virus subtype. In felines, HPAI results in an acute and often fatal course of illness characterized by atypical pneumonia, fever, encephalitis, and multisystem organ failure [2, 39]. H5N1 clade 2.3.4.4b was first reported in felines in 2022, and among the feline infections reported in the literature thus far, it has yielded an extremely high case fatality rate of 90%. We suggest that this an overestimate due to the lack of testing and serosurveys among domestic cats, which accounted for 96.4% of the reported feline cases of clade 2.3.4.4b.

The most prominent symptom of HPAI in felines is acute encephalitis, with neuro invasion often resulting in ataxia, blindness, paralysis, and eventual death. The clinical presentation of encephalitis due to avian influenza is dramatic enough that it is often confused for rabies, likely leading to an underreporting of cases. This pattern is additionally observed in other carnivorous species, such as racoons, foxes, and coyotes, with acute encephalitis being the most common clinical finding [42]. Most surviving animals will have long-term sequelae, particularly resulting in ataxia and seizures. As observed in cats [2], the encephalitis in wild carnivores often results in widespread necrosis evident upon examination of gross pathology, with the presence of cerebral necrosis [42]. Canines are also susceptible to AIV infection, as demonstrated by sporadic cases and deaths [56, 63, 71, 72], as well as a recent H5N1 seropositivity rate of 2% among Washington hunting dogs with intense exposure to waterfowl [73].
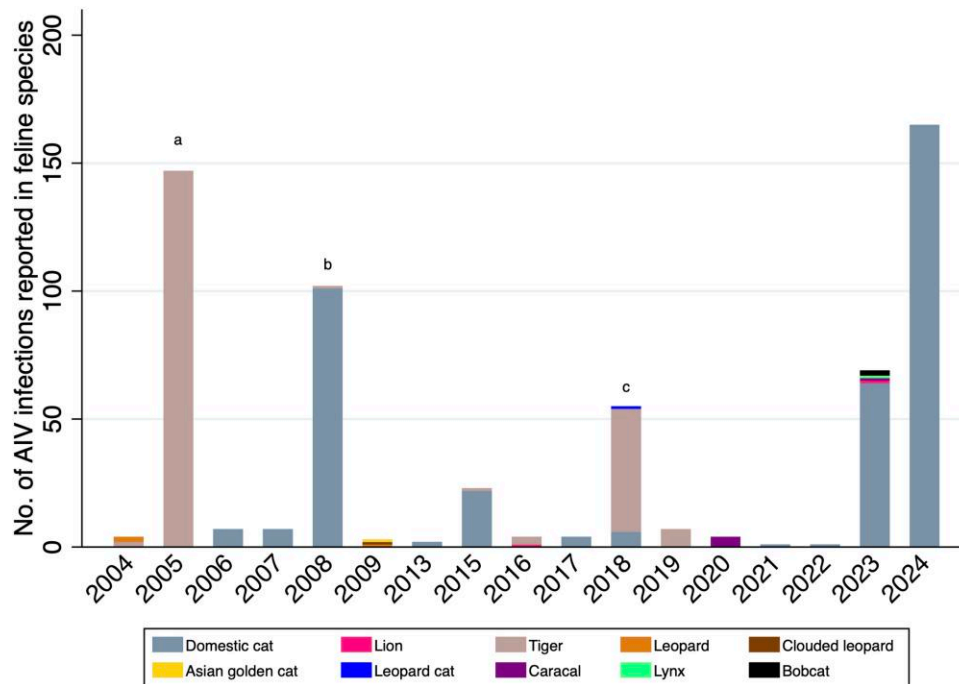
Figure 3. Number of avian influenza virus infections in feline species reported each year in the peer-reviewed literature, 2004–2024. The year published may not be representative of the year in which each of the reported AIV infections occurred. [a]A total of 147 AIV-associated tiger deaths were reported in 2005 from an H5N1 outbreak in a tiger zoo in Thailand in 2004. [b]Approximately 100 of 500 domestic cats sampled in Indonesia were reported to be seropositive for H5N1 (the cited official reports of these tests are difficult to find). [c]Outbreaks of H7N2 among domestic cats occurred in multiple US animal shelters, but data published in the peer-reviewed literature do not include the number of infections and thus they are not included in this figure. Abbreviation: AIV, avian influenza virus.
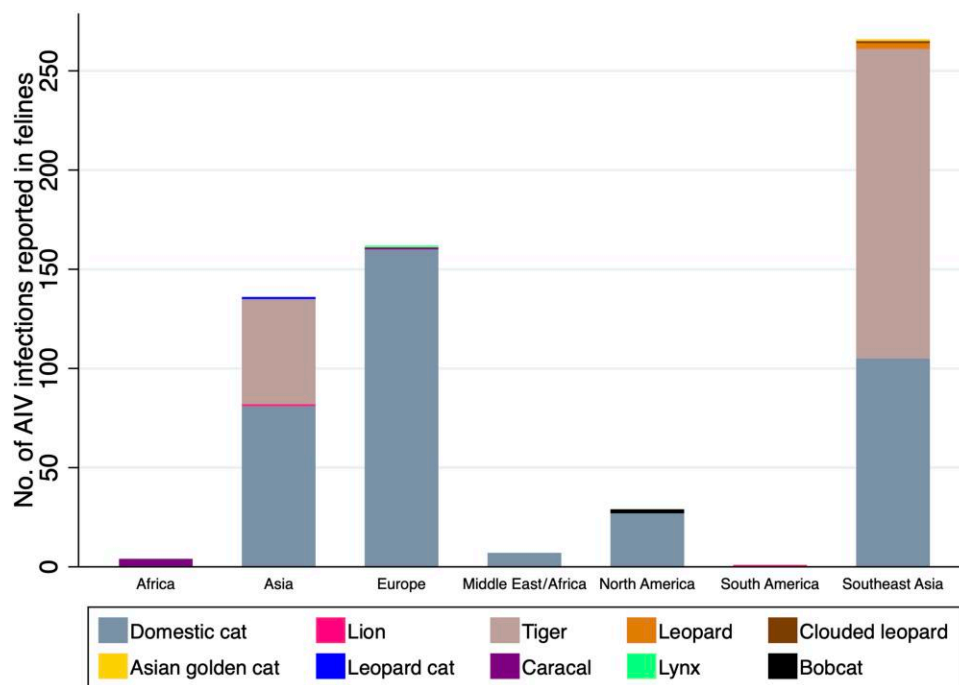

Figure 4. Number of avian influenza virus–associated deaths in felines reported in the peer-reviewed literature, 2004–2024. The year published may not be representative of the year in which each of the reported AIV-associated deaths occurred. One hundred forty-seven AIV-associated tiger deaths were reported in 2005 from an H5N1 outbreak in a tiger zoo in Thailand in 2004. Abbreviation: AIV, avian influenza virus.

Table 2.   RT-PCR-Confirmed Case Fatality Rate of Avian Influenza Virus Subtypes and Clades Identified in Felines From 2004 to 2024

HPAI Subtype	Case Fatality Rate, %		Clade	Case Fatality Rate, %	
	Feline	Domestic Cat		Feline	Domestic Cat
H5N1	71	52.8	Clade 1	0	0
…	…	…	Clade 2.2	100	No infections
…	…	…	Clade 2.3.2	0	No PCR+ cases
…			Clade 2.3.2.1c	100	No infections
			Clade 2.3.2.1b	100	No infections
			Clade 2.3.2.1e	100	No infections
…	…	…	Clade 2.3.4.4b	90	89.6
…	…	…	Clade 2.3.4.4e	100	No infections
H3N8	0	0	…	…	…
H5N6	100	100	…	…	…
H7N2	50	50	…	…	…
H9N2	100	100	C1.2	100	100

Abbreviations: PCR, polymerase chain reaction; RT-PCR, reverse transcription polymerase chain reaction.

Of particular concern is the increase of mammal-to-mammal transmission of avian influenza, indicating further adaptation to mammals. Recently, outbreaks of avian influenza have been reported in a new mammalian host: dairy cattle [2, 49, 74, 75]. This is unusual considering the typical mammalian species affected and the transmission routes previously observed. Much of the infections in mammals have been reported in carnivores or swine, which are omnivorous. The transmission to herbivores is interesting, as avian influenza is often foodborne in mammalian hosts and tends to result from a new host eating an infected host. The infection of ruminants rules out the predation or scavenging route of transmission in this case and suggests that other routes of transmission are occurring, in addition to cattle-to-cattle transmission. Exactly how avian influenza spilled over into dairy cattle is unknown [49, 76]. It is interesting that dairy cattle outbreaks have been uniformly reported as H5N1 clade 2.3.4.4b and have been confined to the United States, which is not the case for other domestic species, including domestic cats. In our review, we identified avian influenza virus infections in felines from 18 countries, of which 8 countries involved H5N1 clade 2.3.4.4b in domestic cats. We speculate that this geographic difference can be partly explained by route of transmission, as cats are carnivorous and prey on species susceptible to avian influenza such as birds and rodents. For example, a serologic study covering a wide range of African wildlife in Namibia demonstrates an association between diet and prior infection with influenza A virus [67]. In total, 21% (15/72) of carnivore-derived serum samples, representing brown and spotted hyenas, honey badgers, black-backed jackals, bat-eared foxes, African wild dogs, lions, leopards, cheetahs, and caracals, were seropositive for hemagglutinin. Likewise, 44% (11/25) of the species that commonly prey on birds, including jackals, caracals, and honey badgers, were seropositive [67]. In contrast, only 5% (2/39) of herbivorous species serum samples were seropositive for hemagglutinin

[67]. These 2 cases consisted of a single wildebeest seropositive for both H4 and H11 and a single black rhinoceros weakly seropositive for H5 [67]. However, a more recent serologic study of other herbivorous species in Pakistan demonstrates high seroprevalence of HPAI H5, with 27% of goats and 34% of sheep testing seropositive for clade 2.3.2.1c and 24% of goats and 31% of sheep testing seropositive for 2.3.4.4b [77]. This study also tested for H7 and H9, with 14% of goats and 37% of sheep seropositive for H7 and 17% of goats and 35% of sheep seropositive for H9. This new finding sets the stage for further surveillance and characterization of avian influenza virus infections among these domestic species, especially since the first known HPAI cases in US ruminant livestock were among newborn goats infected with H5N1 clade 2.3.4.4b in February 2024 [78]—shortly before outbreaks among US dairy cattle were reported. The newborn goat cases were presumed to be the result of direct spillover from nearby infected poultry. However, specific routes of transmission (eg, foodborne, airborne) should be explored.

Most of the reported AIV infections in felines were confirmed or suspected to be a result of eating dead pigeons, chickens, and other birds, as well as contaminated raw chicken feed. The first reported foodborne-related instances involved outbreaks of H5N1 in tiger and leopard zoos and breeding operations in Thailand [7, 10], which resulted in a large number of tiger deaths in 2004 [7]. The outbreaks were suspected to have started via infected chickens served to the tigers. The tigers were primarily fed whole, raw chicken carcasses, and at least 1 chicken carcass tested positive for H5N1 during the investigations. A similar outbreak of H5N1 also occurred at a wildlife rescue center in Cambodia in 2004 [17]. In this outbreak, a multitude of animals became infected, most notably several feline species, as well as several species of carnivorous birds. All were reported to have been fed chickens, although it was not specified if the feeder chickens were provided dead or alive.
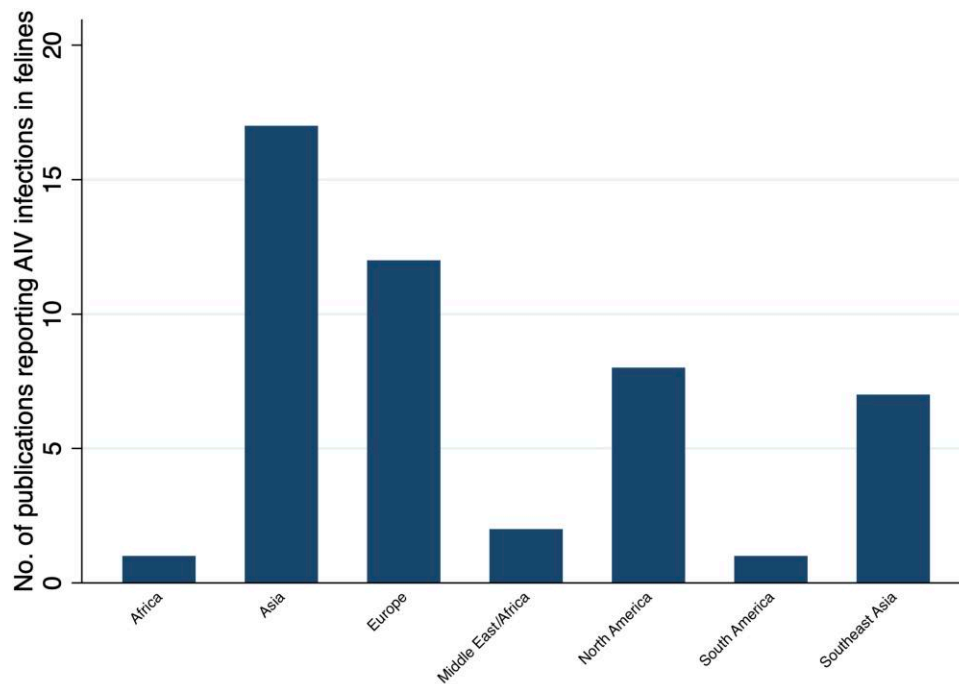
Figure 5. Geographical distribution of avian influenza virus infections reported in feline species, 2004–2024. Abbreviation: AIV, avian influenza virus.

Considering that the outbreak among the carnivores ceased when the chickens were withdrawn as food, it was deemed that the outbreak was likely foodborne. More recently, foodborne transmission was suspected in AIV outbreaks among domestic cats in Poland in summer 2023 [38, 39]. Culture-positive avian influenza virus was derived from a chicken sample from the freezer of the owners who fed such meat to 1 of the infected cats. As the 2023 feline outbreak in Poland coincided with an in-country poultry outbreak of H5N1 clade 2.3.4.4b, initial suspicions may have centered on predation or interactions with live birds as a means of transmission. However, as the outbreaks involved both indoor and outdoor felines, foodborne transmission of AIV was considered. As a result, frozen poultry samples were tested and found to be positive by MDCK cell culture. Illumina sequencing was performed, and the frozen poultry samples were differentiated from feline isolates by a maximum of 2 nucleotides per strand [38]. Two additional foodborne-related outbreaks of H5N1 clade 2.3.4.4b occurred in South Korea cat shelters in summer 2023 [45, 46]. Improperly sterilized duck meat was implicated in both outbreaks [46].

In addition to predation and consumption of contaminated meat, a new phenomenon has emerged where domestic cats are being infected with H5N1 through the consumption of contaminated raw milk from US dairy farms. H5N1 detections have also been reported in house and deer mice in New Mexico, Colorado, and Washington [70], which could potentially serve as an additional route of transmission to domestic

cats. Interestingly, cases of H5N1 clade 2.3.4.4b recently reported by the Colorado Health Department included 2 indoor-only domestic cats with no known exposure to infected animals [79]. This observation raises concerns regarding new and unknown transmission routes of AIV to domestic cats. The USDA reports ~96 HPAI H5 detections in felines from 2022 to present [70], of which ~20 have been reported in the scientific literature. Thus, important clinical, demographic, and sequencing data are unknown or unavailable for the majority of US feline cases.

Our review was limited by the underreporting of avian influenza infections in felines in the scientific literature. Due to underreporting, our case count is an underestimate of the actual impact of avian influenza in feline hosts, and our estimated case fatality rates are likely an overestimate. Felines are not typically monitored for avian influenza, and testing is usually performed postmortem if at all. When a domestic feline or captive wild feline arrives at a clinic presenting with symptoms, such as severe atypical pneumonia, fever, and neurological problems such as ataxia and blindness, avian influenza is not usually suspected. As avian influenza is an unusual diagnosis and symptomatic cats would typically be euthanized to contain spread or for humane reasons, testing is of little benefit to the individual patient. However, from a One Health perspective, testing is highly valuable and can provide insight into nearby avian influenza outbreaks, as well as the potential risk of zoonotic spillover. Based on the avian influenza seropositivity of various felines in some of the studies we reviewed, we estimate that

feline cases are markedly underreported in the literature. Additionally, testing feline patients for AIV is not a routine practice as treatment options are limited under most circumstances. While it is often required that cases of HPAI be reported to public health authorities, subtype and clade are often not confirmed. As a result, several publications do not report the AIV subtype or clade. However, recent and ongoing outbreaks of H5N1 clade 2.3.4.4b among dairy cattle in the United States, representing a significant threat to farm cats [2], have prompted multiple states to begin postmortem H5N1 testing among rabies-negative domestic cats. However, subclinical infections of H5N1 in domestic cats do occur [3], including asymptomatic infections of clade 2.3.4.4b [4]. Thus, we argue that wider surveillance among domestic cats is urgently needed to determine how widespread the virus is in order to appropriately assess the risk of spillover to humans and other animals. As feline-to-human transmission of AIV has been documented [7–9] and potential airborne and fomite-mediated transmission implicated [68], farm and free-roaming cat owners, veterinarians, zoo keepers, and animal shelter volunteers may have a heightened risk of AIV infection during epizootics among birds and mammals.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

References

1. Sillman SJ, Drozd M, Loy D, Harris SP. Naturally occurring highly pathogenic avian influenza virus H5N1 clade 2.3.4.4b infection in three domestic cats in North America during 2023. J Comp Pathol 2023; 205:17–23.
2. Burrough ER, Magstadt DR, Petersen B, et al. Highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus infection in domestic dairy cattle and cats, United States, 2024. Emerg Infect Dis 2024; 30:1335–43.
3. Leschnik M, Weikel J, Möstl K, et al. Subclinical infection with avian influenza A H5N1 virus in cats. Emerg Infect Dis 2007; 13:243.
4. Moreno A, Bonfante F, Bortolami A, et al. Asymptomatic infection with clade 2.3.4.4b highly pathogenic avian influenza A(H5N1) in carnivore pets, Italy, April 2023. Euro Surveill 2023; 28:2300441.
5. Kuiken T, Rimmelzwaan G, van Riel D, et al. Avian H5N1 influenza in cats. Science 2004; 306:241.
6. Hatta M, Zhong G, Gao Y, et al. Characterization of a feline influenza A(H7N2) virus. Emerg Infect Dis 2018; 24:75–86.
7. Thanawongnuwech R, Amonsin A, Tantilertcharoen R, et al. Probable tiger-to-tiger transmission of avian influenza H5N1. Emerg Infect Dis 2005; 11:699–701.
8. Lee CT, Slavinski S, Schiff C, et al. Outbreak of influenza A(H7N2) among cats in an animal shelter with cat-to-human transmission—New York City, 2016. Clin Infect Dis 2017; 65:1927–9.
9. Poirot E, Levine MZ, Russell K, et al. Detection of avian influenza A(H7N2) virus infection among animal shelter workers using a novel serological approach—New York City, 2016–2017. J Infect Dis 2019; 219:1688–96.
10. Keawcharoen J, Oraveerakul K, Kuiken T, et al. Avian influenza H5N1 in tigers and leopards. Emerg Infect Dis 2004; 10:2189–91.
11. Further spread of avian influenza in Europe, detection in French farmed birds and German cat. Euro Surveill 2006; 11:2911.
12. Songserm T, Amonsin A, Jam-on R, et al. Avian influenza H5N1 in naturally infected domestic cat. Emerg Infect Dis 2006; 12:681–3.
13. Yingst SL, Saad MD, Felt SA. Qinghai-like H5N1 from domestic cats, Northern Iraq. Emerg Infect Dis 2006; 12:1295–7.
14. Klopfleisch R, Wolf PU, Uhl W, et al. Distribution of lesions and antigen of highly pathogenic avian influenza virus A/Swan/Germany/R65/06 (H5N1) in domestic cats after presumptive infection by wild birds. Vet Pathol 2007; 44:261–8.
15. Mushtaq MH, Juan H, Jiang P, et al. Complete genome analysis of a highly pathogenic H5N1 influenza A virus isolated from a tiger in China. Arch Virol 2008; 153:1569–74.
16. Lam TT-Y, Hon C-C, Pybus OG, et al. Evolutionary and transmission dynamics of reassortant H5N1 influenza virus in Indonesia. PLoS Pathog 2008; 4:e1000130.
17. Desvaux S, Marx N, Ong S, et al. Highly pathogenic avian influenza virus (H5N1) outbreak in captive wild birds and cats, Cambodia. Emerg Infect Dis 2009; 15:475–8.
18. El-Sayed A, Prince A, Fawzy A, et al. Sero-prevalence of avian influenza in animals and human in Egypt. Pak J Biol Sci 2013; 16:524–9.
19. He S, Shi J, Qi X, Huang G, Chen H, Lu C. Lethal infection by a novel reassortant H5N1 avian influenza A virus in a zoo-housed tiger. Microbes Infect 2015; 17:54–61.
20. Zhou H, He S, Sun L, et al. Serological evidence of avian influenza virus and canine influenza virus infections among stray cats in live poultry markets, China. Vet Microbiol 2015; 175:369–73.
21. Sun L, Zhou P, He S, et al. Sparse serological evidence of H5N1 avian influenza virus infections in domestic cats, Northeastern China. Microb Pathog 2015; 82:27–30.
22. Yu Z, Gao X, Wang T, et al. Fatal H5N6 avian influenza virus infection in a domestic cat and wild birds in China. Sci Rep 2015; 5:10704.
23. Zhao F-R, Zhou D-H, Zhang Y-G, et al. Detection prevalence of H5N1 avian influenza virus among stray cats in Eastern China. J Med Virol 2015; 87:1436–40.
24. Hu T, Zhao H, Zhang Y, et al. Fatal influenza A (H5N1) virus infection in zoo-housed tigers in Yunnan Province, China. Sci Rep 2016; 6:25845.
25. Chen Q, Wang H, Zhao L, et al. First documented case of avian influenza (H5N1) virus infection in a lion. Emerg Microbes Infect 2016; 5:e125.
26. Newbury SP, Cigel F, Killian ML, et al. First detection of avian lineage H7N2 in *Felis catus*. Genome Announc 2017; 5:e00457-17.
27. Cao X, Yang F, Wu H, Xu L. Genetic characterization of novel reassortant H5N6-subtype influenza viruses isolated from cats in Eastern China. Arch Virol 2017; 162:3501–5.
28. Mahardika G. Surveillance of avian influenza virus of H5N1 subtype in backyard animals and its introduction in Bali, Indonesia. PVJ 2018; 38:7–12.
29. Kim HK, Kim H-J, Noh JY, et al. Serological evidence of H5-subtype influenza A virus infection in indigenous avian and mammalian species in Korea. Arch Virol 2018; 163:649–57.
30. Wang K, Wang H, Feng N, et al. Serological surveillance of avian influenza virus and canine distemper virus in captive Siberian tigers in Northeastern China. Pol J Vet Sci 2018; 21:491–5.
31. Lee K, Lee E-K, Lee H, et al. Highly pathogenic avian influenza A(H5N6) in domestic cats, South Korea. Emerg Infect Dis 2018; 24:2343–7.
32. Sangkachai N, Thongdee M, Chaiwattanarungruengpaisan S, et al. Serological evidence of influenza virus infection in captive wild felids, Thailand. J Vet Med Sci 2019; 81:1341–7.
33. Soilemetzidou E-S, De Bruin E, Franz M, et al. Diet may drive influenza A virus exposure in African mammals. J Infect Dis 2020; 221:175–82.
34. Zhao J, He W, Lu M, He H, Lai A. Emergence and characterization of a novel reassortant canine influenza virus isolated from cats. Pathogens 2021; 10:1320.

35. Bao P, Liu Y, Zhang X, et al. Human infection with a reassortment avian influenza A H3N8 virus: an epidemiological investigation study. Nat Commun **2022**; 13: 6817.

36. Tammiranta N, Isomursu M, Fusaro A, et al. Highly pathogenic avian influenza A (H5N1) virus infections in wild carnivores connected to mass mortalities of pheasants in Finland. Infect Genet Evol **2023**; 111:105423.

37. Briand F-X, Souchaud F, Pierre I, et al. Highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in domestic cat, France, 2022. Emerg Infect Dis **2023**; 29:1696–8.

38. Rabalski L, Milewska A, Pohlmann A, et al. Emergence and potential transmission route of avian influenza A (H5N1) virus in domestic cats in Poland, June 2023. Euro Surveill **2023**; 28:2300390.

39. Domańska-Blicharz K, Świętoń E, Świątalska A, et al. Outbreak of highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in cats, Poland, June to July 2023. Euro Surveill **2023**; 28:2300366.

40. Szaluś-Jordanow O, Golke A, Dziecątkowski T, et al. A fatal A/H5N1 avian influenza virus infection in a cat in Poland. Microorganisms **2023**; 11:2263.

41. Yang J, Yan J, Zhang C, et al. Genetic, biological and epidemiological study on a cluster of H9N2 avian influenza virus infections among chickens, a pet cat, and humans at a backyard farm in Guangxi, China. Emerg Microbes Infect **2023**; 12:2143282.

42. Elsmo EJ, Wünschmann A, Beckmen KB, et al. Highly pathogenic avian influenza A(H5N1) virus clade 2.3.4.4b infections in wild terrestrial mammals, United States, 2022. Emerg Infect Dis **2023**; 29:2451–60.

43. Cruz CD, Icochea ME, Espejo V, et al. Highly pathogenic avian influenza A(H5N1) from wild birds, poultry, and mammals, Peru. Emerg Infect Dis **2023**; 29:2572–6.

44. Villanueva-Saz S, Martínez M, Rueda P, et al. Serological exposure to influenza A in cats from an area with wild birds positive for avian influenza. Zoonoses Public Health **2024**; 71:324–30.

45. Lee K, Yeom M, Vu TTH, et al. Characterization of highly pathogenic avian influenza A (H5N1) viruses isolated from cats in South Korea, 2023. Emerg Microbes Infect **2024**; 13:2290835.

46. Kang Y-M, Heo G-B, An S-H, et al. Highly pathogenic avian influenza A(H5N1) virus infection in cats, South Korea, 2023. Emerg Infect Dis **2024**; 30:2510–20.

47. Cavicchio L, Campalto M, Carrino M, et al. Influenza in feral cat populations: insights from a study in North-East Italy. Front Vet Sci **2024**; 11:1439354.

48. Duijvestijn MBHM, Schuurman NNMP, Vernooij JCM, et al. Highly pathogenic avian influenza (HPAI) H5 virus exposure in domestic cats and rural stray cats, The Netherlands, October 2020 to June 2023. Euro Surveill **2024**; 29:2400326.

49. Caserta LC, Frye EA, Butt SL, et al. Spillover of highly pathogenic avian influenza H5N1 virus to dairy cattle. Nature **2024**; 634:669–76.

50. Chothe SK, Srinivas S, Misra S, et al. Marked neurotropism and potential adaptation of H5N1 clade 2.3.4.4.b virus in naturally infected domestic cats. Emerg Microbes Infect **2025**; 14:2440498.

51. Mainenti M, Siepker C, Magstadt DR, et al. Distribution of lesions and detection of influenza A(H5N1) virus, clade 2.3.4.4b, in ante- and postmortem samples from naturally infected domestic cats on U.S. dairy farms. J VET Diagn Invest **2024**; 37:27–35.

52. Hinshaw VS, Webster RG, Easterday BC, Bean WJ. Replication of avian influenza A viruses in mammals. Infect Immun **1981**; 34:354–61.

53. Rimmelzwaan GF, van Riel D, Baars M, et al. Influenza A virus (H5N1) infection in cats causes systemic disease with potential novel routes of virus spread within and between hosts. Am J Pathol **2006**; 168:176–83, quiz 364.

54. van Riel D, Munster VJ, de Wit E, et al. H5n1 virus attachment to lower respiratory tract. Science **2006**; 312:399.

55. Chang S, Ding Z, Yang S-T, et al. Study on the histopathology of cats inoculated with H5N1 subtype high pathogenic avian influenza virus originated from tigers [in Chinese]. Bing Du Xue Bao **2007**; 23:477–80.

56. Giese M, Harder TC, Teifke JP, et al. Experimental infection and natural contact exposure of dogs with avian influenza virus (H5N1). Emerg Infect Dis **2008**; 14: 308–10.

57. Vahlenkamp TW, Harder TC, Giese M, et al. Protection of cats against lethal influenza H5N1 challenge infection. J Gen Virol **2008**; 89:968–74.

58. Marschall J, Schulz B, Hartmann K. Evaluation of a point-of-care influenza antigen test for the detection of highly pathogenic avian influenza H5N1 virus in cats. Transbound Emerg Dis **2008**; 55:315–7.

59. van Riel D, Rimmelzwaan GF, van Amerongen G, Osterhaus ADME, Kuiken T. Highly pathogenic avian influenza virus H7N7 isolated from a fatal human case causes respiratory disease in cats but does not spread systemically. Am J Pathol **2010**; 177:2185–90.

60. Vahlenkamp TW, Teifke JP, Harder TC, Beer M, Mettenleiter TC. Systemic influenza virus H5N1 infection in cats after gastrointestinal exposure. Influenza Other Respir Viruses **2010**; 4:379–86.

61. Reperant LA, van de Bildt MWG, van Amerongen G, et al. Marked endotheliotropism of highly pathogenic avian influenza virus H5N1 following intestinal inoculation in cats. J Virol **2012**; 86:1158–65.

62. Driskell EA, Jones CA, Berghaus RD, Stallknecht DE, Howerth EW, Tompkins SM. Domestic cats are susceptible to infection with low pathogenic avian influenza viruses from shorebirds. Vet Pathol **2013**; 50:39–45.

63. Zhang K, Zhang Z, Yu Z, et al. Domestic cats and dogs are susceptible to H9N2 avian influenza virus. Virus Res **2013**; 175:52–7.

64. Kim Y-I, Pascua PNQ, Kwon H-I, et al. Pathobiological features of a novel, highly pathogenic avian influenza A(H5N8) virus. Emerg Microbes Infect **2014**; 3:e75.

65. Tabynov K, Sansyzbay A, Sandybayev N, Mambetaliyev M. The pathogenicity of swan derived H5N1 virus in birds and mammals and its gene analysis. Virol J **2014**; 11:207.

66. Kim HM, Park EH, Yum J, Kim HS, Seo SH. Greater virulence of highly pathogenic H5N1 influenza virus in cats than in dogs. Arch Virol **2015**; 160:305–13.

67. Wang L, Fu X, Zheng Y, et al. The NS1 protein of H5N6 feline influenza virus inhibits feline beta interferon response by preventing NF-κB and IRF3 activation. Dev Comp Immunol **2017**; 74:60–8.

68. Blachere FM, Lindsley WG, Weber AM, et al. Detection of an avian lineage influenza A(H7N2) virus in air and surface samples at a New York City feline quarantine facility. Influenza Other Respir Viruses **2018**; 12:613–22.

69. Cui P, Shi J, Wang C, et al. Global dissemination of H5N1 influenza viruses bearing the clade 2.3.4.4b HA gene and biologic analysis of the ones detected in China. Emerg Microbes Infect **2022**; 11:1693–704.

70. USDA Animal and Plant Health Inspection Service. HPAI detections in mammals. Available at: https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/mammals. Accessed November 19, 2024.

71. Songserm T, Amonsin A, Jam-on R, et al. Fatal avian influenza A H5N1 in a dog. Emerg Infect Dis **2006**; 12:1744.

72. Szaluś-Jordanow O, Golke A, Dziecątkowski T, et al. Upper respiratory tract disease in a dog infected by a highly pathogenic avian A/H5N1 virus. Microorganisms **2024**; 12:689.

73. Brown JD, Black A, Haman KH, et al. Antibodies to influenza A(H5N1) virus in hunting dogs retrieving wild fowl, Washington, USA. Emerg Infect Dis **2024**; 30: 1271–4.

74. Oguzie JU, Marushchak LV, Shittu I, et al. Avian influenza A(H5N1) virus among dairy cattle, Texas, USA. Emerg Infect Dis **2024**; 30:1425–9.

75. Garg S. Outbreak of highly pathogenic avian influenza A(H5N1) viruses in U.S. dairy cattle and detection of two human cases—United States, 2024. MMWR Morb Mortal Wkly Rep **2024**; 73:501–5.

76. Peacock T, Moncla L, Dudas G, et al. The global H5N1 influenza panzootic in mammals. Nature. **2025**; 637:304–313. https://doi.org/10.1038/s41586-024-08054-z

77. Wong FY, Yaqub T, Zhang R, et al. Highly pathogenic avian influenza H5 virus exposure in goats and sheep. bioRxiv 2024.08.31.610397 [Preprint]. August 31, 2024. Available at: https://www.biorxiv.org/content/10.1101/2024.08.31.610397v1. Accessed November 19, 2024.

78. Callahan D. Stevens County goat tests positive for same influenza virus affecting poultry. *Minnesota Board* of Animal Health. March 20, 2024. Available at: https://www.bah.state.mn.us/news_release/stevens-county-goat-tests-positive-for-same-influenza-virus-affecting-poultry. Accessed November 19, 2024.

79. Moore K. Influenza A (Highly Pathogenic Avian Influenza H5N1) in Domestic Cats. CVMA; **2024**.