Avian Influenza

Fowl Plague, Grippe Aviaire

Last Updated: November 2015

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY®
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: 515.294.7189
Fax: 515.294.8259
cfsph@iastate.edu
www.cfsph.iastate.edu

INSTITUTE FOR INTERNATIONAL COOPERATION IN ANIMAL BIOLOGICS
Iowa State University
College of Veterinary Medicine
www.cfsph.iastate.edu/IICAB/

Importance

Avian influenza viruses are highly contagious, extremely variable viruses that are widespread in birds. Wild birds in aquatic habitats are thought to be their natural reservoir hosts, but domesticated poultry and other birds can also be infected.[1-9] Most viruses cause only mild disease in poultry, and are called low pathogenic avian influenza (LPAI) viruses. Highly pathogenic avian influenza (HPAI) viruses can develop from certain LPAI viruses, usually while they are circulating in poultry flocks.[10] HPAI viruses can kill up to 90-100% of the flock, and cause epidemics that may spread rapidly, devastate the poultry industry and result in severe trade restrictions.[2,11,12] In poultry, the presence of LPAI viruses capable of evolving into HPAI viruses can also affect international trade.[11]

Avian influenza viruses can occasionally affect mammals, including humans, usually after close contact with infected poultry. While infections in people are often limited to conjunctivitis or mild respiratory disease, some viruses can cause severe illness. In particular, Asian lineage H5N1 HPAI viruses have caused rare but life-threatening infections, now totaling nearly 850 laboratory-confirmed cases since 1997,[13] and H7N9 LPAI viruses have caused more than 600 serious human illnesses in China since 2013.[14-16] Avian influenza viruses can also infect other species of mammals, sometimes causing severe or fatal disease.[12,17-43] In rare cases, avian influenza viruses can become adapted to circulate in a mammalian species. During the last century, such viruses have caused or contributed to at least three pandemics in humans, contributed to the diversity of swine influenza viruses in pigs, and also produced one of the two canine influenza viruses now circulating among dogs.[1,44,45,45-57]

Etiology

Avian influenza results from infection by viruses belonging to the species *influenza A virus*, genus *influenzavirus A* and family Orthomyxoviridae. These viruses are also called type A influenza viruses. Influenza A viruses are classified into subtypes based on two surface proteins, the hemagglutinin (HA) and neuraminidase (NA). A virus that has a type 1 HA and type 2 NA, for example, would have the subtype H1N2. At least 16 hemagglutinins (H1 to H16), and 9 neuraminidases (N1 to N9) have been found in viruses from birds, while two additional HA and NA types have been identified, to date, only in bats.[2,6,12,58-60] Some hemagglutinins, such as H14 and H15, seem to be uncommon, or perhaps are maintained in wild bird species or locations that are not usually sampled.[7]

Avian influenza viruses are classified as either low pathogenic (also called low pathogenicity) avian influenza viruses or highly pathogenic (high pathogenicity) avian influenza viruses. A virus is defined as HPAI or LPAI by its ability to cause severe disease in intravenously inoculated young chickens in the laboratory, or by its possession of certain genetic features that have been associated with high virulence in HPAI viruses (i.e., the sequence at the HA cleavage site).[2,58] HPAI viruses usually cause severe disease in chicken and turkey flocks, while LPAI infections are generally much milder in all avian species. With rare exceptions, HPAI viruses found in nature have always contained the H5 or H7 hemagglutinin.[10,61-63] Two exceptions were H10 viruses that technically fit the HPAI definition if they were injected directly into the bloodstream of chickens, but caused only mild illness in birds that became infected by the respiratory (intranasal) route.[62] Another H10 virus also fit the HPAI definition; however, this virus affected the kidneys and had a high mortality rate in intranasally inoculated young chickens.[64] In the laboratory, the insertion of genetic sequences from HPAI viruses into non-H7, non-H5 viruses has created some viruses that are pathogenic only after intravenous inoculation, and other viruses (containing H2, H4, H8 or H14) that were highly virulent after both intravenous and intranasal inoculation.[65] Recently, an H4N2 virus with a genetic signature characteristic of HPAI viruses was isolated from a flock of naturally infected quail.[66] It was a LPAI virus, with low virulence when inoculated into chickens.

In rare cases, an H5 or H7 virus has a genetic signature that classifies it as an HPAI virus, but causes only mild illness in poultry.[67,68] Such viruses may have been isolated when they were evolving to become more virulent. Their presence triggers the same regulatory responses as fully virulent HPAI viruses.

Antigenic shift and drift in influenza A viruses

The viral HA, and to a lesser extent the NA, are major targets for the immune response, and there is ordinarily little or no cross-protection between different HA or NA types.[69-78] Influenza A viruses are very diverse, and two viruses that share a subtype may be only distantly related. The high variability is the result of two processes, mutation and genetic reassortment. Mutations cause gradual changes in the HA and NA proteins of the virus, a process called 'antigenic drift.'[79] Once these proteins have changed enough, immune responses against the former HA and NA may no longer be protective.

Genetic reassortment can cause more rapid changes. The influenza A genome consists of 8 individual gene segments,[76,77] and when two different viruses infect the same cell, gene segments from both viruses may be packaged into a single, novel virion. This can occur whenever two influenza viruses replicate in the same cell, whether the viruses are adapted to the same host species (e.g., two different avian influenza viruses) or originally came from different hosts (for instance, an avian influenza virus and a swine influenza virus). An important aspect of reassortment is that it can generate viruses containing either a new HA, a new NA, or both. Such abrupt changes, called 'antigenic shifts,' may be sufficient for the novel virus to completely evade existing immunity. After a subtype has become established in a species and has circulated for a time, antigenic shifts and drift can produce numerous viral variants.

Avian influenza virus lineages

There are two well-recognized lineages of avian influenza viruses, Eurasian and North American.[7] As implied by the names, Eurasian lineage viruses primarily circulate among birds in Eurasia, and North American lineage viruses in the Americas. The amount of reassortment between these lineages seems to differ between regions, with very few reassortant viruses detected in some areas or wild bird populations, but significant reassortment where there is overlap between migratory flyways, such as in Alaska and Iceland.[7,80-92] Viruses in wild birds (or portions of viruses) are more likely to be transferred between hemispheres in the latter regions. Avian influenza virus surveillance in Central and South America has been limited, but the viruses detected include a unique South American sublineage (or lineage) as well as viruses closely related to the North American lineage.[93,94] The viruses in New Zealand and Australia might be geographically isolated to some extent, although there is also evidence of mixing with viruses from other areas.[95-97]

Transfer of influenza viruses between species

Although influenza A viruses are adapted to circulate in a particular host or hosts, they can occasionally infect other species. In most cases, the virus cannot be transmitted efficiently between members of that species, and soon disappears.[1,5,12,31,45,50,79,98-104] On rare occasions, however, a virus continues to circulate in the new host, either "whole" or after reassorting with another influenza virus.[45,46,50-55,57,101,105,106] Some influenza A viruses have become adapted to circulate in pigs (swine influenza viruses), horses (equine influenza viruses), humans (human influenza A viruses) and dogs (canine influenza viruses). The ancestors of these viruses are thought to have originated in birds, either in the distant past or more recently.[1-5,7,50,51,107] Further information about virus transmission between species can be found in the 'Influenza' factsheet.

Species Affected

Wild birds

The vast majority of LPAI viruses are maintained in asymptomatic wild birds, particularly birds in wetlands and other aquatic habitats, which are thought to be their natural reservoir hosts.[1-9] Some species may maintain viruses long-term, while others might be spillover hosts. Infections are particularly common among members of the order Anseriformes (waterfowl, such as ducks, geese and swans) and two families within the order Charadriiformes, the Laridae (gulls and terns) and Scolopacidae (shorebirds).[1-3,5-9,46,84,89,108-112] However, infections may be uncommon in some members of these orders. Within the Laridae, viruses tend to occur more often in gulls than terns.[9] The prevalence of infection among wading birds (waders) is reported to be high in some areas, but low in others.[92,96,108] Aquatic species belonging to other orders occasionally have high infection rates, and might also be involved in the epidemiology of this disease.[9,113,114; 115 cited in 114] For instance, infections among seabirds seem to be particularly common in murres (*Uria* spp.).[116]

The most common influenza subtypes in wild birds may differ between species and regions, and can change over time.[7,110,111,114,116-118] Migrating birds, which can fly long distances, may exchange viruses with other populations at staging, stopover or wintering sites.[7] Virus diversity seems to be particularly high among charadriform birds.[7,108] A few avian influenza subtypes seem to have a limited host range. Examples include H13 and H16 viruses, which have mainly been found in gulls and terns, and H14 viruses, which have been detected rarely and only in a few species.(i.e., in a few ducks, sea ducks and a herring gull).[7,80,84,111,119-125] Such viruses may rarely (or never) be transferred to poultry.

LPAI viruses can also infect wild birds that live on land (terrestrial birds), such as raptors and passerines, but under ordinary conditions, infections seem to be uncommon in these species, and they are not thought to be important reservoirs.[8,9,126-135] Higher infection rates are occasionally reported in individual species, and in a study from Vietnam, viruses were particularly common in some terrestrial birds that forage in flocks, with an especially high prevalence in Japanese White-eyes (*Zosterops japonicus*).[128,134] Similarly, a recent study from Central and West Africa detected influenza virus RNA in an unusually high percentage of passerine birds.[136]

HPAI viruses are not usually found in wild birds, although they may be isolated transiently near outbreaks in poultry.[130] Exceptions include the Asian lineage H5N1 viruses and some of their reassortants (e.g., H5N8 viruses), which have been found repeatedly in wild birds, an H5N3 virus isolated from an outbreak among terns in the 1960s, an H7N1 virus that was isolated from a sick wild siskin, *Carduelis spinus*, and an H5N2 virus found in a few asymptomatic wild ducks and geese in Africa.[27,32,107,137-163]

Domesticated birds and mammals

When LPAI viruses from wild birds are transferred to poultry, the viruses may circulate inefficiently and die out; become adapted to the new host and continue to circulate as LPAI viruses; or if they contain H5 or H7, they may evolve into HPAI viruses.[4,10,12] Once a virus has adapted to poultry, it rarely re-establishes itself in wild birds.[10] HPAI and LPAI viruses have been found in many domesticated birds, including gallinaceous poultry and game birds, ducks, geese, ratites, pigeons and cage birds; however, some species seem to be more resistant to infection and/or illness than others.[2,27,72,145,146,148-150,164-189] For example, there are few reports of infections in psittacine birds, and pigeons appear to be relatively resistant to infection compared to poultry.

Avian influenza virus infections have been detected occasionally in numerous species of mammals. Some of these species include cats, dogs, pigs, horses, donkeys, mink, and various wild and captive wild mammals.[12,20-35,37,40,43,98,190-203] Ferrets can be infected experimentally with many viruses.

Important viral lineages and susceptible species

Poultry can be infected by many different LPAI and HPAI viruses, belonging to multiple subtypes, but three viral lineages are currently of particular concern. Some of these viruses have also been reported in mammals.

Host range of the Asian lineage H5N1 avian influenza viruses and reassortants including H5N8

The A/goose/Guangdong/1996 lineage (‘Asian lineage’) of H5N1 HPAI viruses first emerged among poultry in China in the late 1990s, and has become widespread and very diverse.[12,204-210] Some variants of H5N1 differ in their virulence for mammals and/or birds.[149,209,211] HPAI H5N2, H5N5, H5N6 and H5N8 viruses, resulting from reassortment between Asian lineage H5N1 viruses and other avian influenza viruses, have been reported among poultry in Asia.[212-218] H5N8 viruses became widespread among birds in Asia and Europe in 2014.[157,219] They reached North America in late 2014, and have reassorted with North American lineage viruses to produce unique variants of other subtypes such as H5N1 and H5N2.[156,158-160,219-223]

Whether wild birds can maintain Asian lineage H5 viruses for long periods (or indefinitely), or are repeatedly infected from poultry, is still controversial.[142,147,154,224-226] However, the evidence that wild birds can transfer H5N1 HPAI viruses and some of their reassortants (e.g., H5N8) to new geographic regions now appears strong [137,138,156,157,157-159,219,226]

Asian lineage H5N1 HPAI viruses seem to have an unusually wide host range. These viruses can infect a wide variety of wild birds belonging to many different orders, including the Anseriformes and Charadriiformes.[27,32,107,142-155] Both clinical cases and asymptomatic infections have been described.[27,151,154,163,227] These viruses can also infect many species of mammals, and their full host range is probably not yet known. They have been found in pigs, cats, dogs, donkeys, tigers (*Panthera tigris*), leopards (*Panthera pardus*), clouded leopards (*Neofelis nebulos*), lions (*Panthera leo*), Asiatic golden cats (*Catopuma temminckii*), stone martens (*Mustela foina*), raccoon dogs (*Nyctereutes procyonoides*), palm civets (*Chrotogale owstoni*), plateau pikas (*Ochotona curzoniae*) and a wild mink (*Mustela vison*).[12,17-37] Serological evidence of infection or exposure has also been reported in horses and raccoons.[20,228-230] Experimental infections have been established in cats, dogs, foxes, pigs, ferrets, laboratory rodents, cynomolgus macaques (*Macaca fascicularis*) and rabbits.[17,27,31,34,107,150,191,211,231-239] Cattle could be experimentally infected with viruses isolated from cats,[239] but studies in Egypt detected no antibodies to H5N1 viruses in cattle, buffalo, sheep or goats, suggesting that these species are not normally infected.[228]

Some Asian lineage H5 reassortants, such as an H5N2 virus isolated recently from a dog with respiratory signs, may be able to cause illness in mammals.[40-42] This H5N2 virus could be transmitted from experimentally infected dogs to dogs, chickens and cats.[40-42] There have been no reports of illnesses caused by Asian lineage H5N8 viruses in mammals, as of November 2015, although seropositive dogs were detected on some infected farms in Asia.[240]. Initial laboratory experiments in ferrets and mice reported low to moderate virulence in these species, suggesting that the currently circulating H5N8 viruses may be less pathogenic for mammals than some H5N1 isolates.[240-242] In another study, virus replication was inefficient in experimentally infected dogs, which developed no clinical signs.[240] Cats were more likely to become infected, and had mild and transient signs. Asian lineage H5N6 viruses have, to date, been isolated from apparently healthy pigs.[39]

Host range of Eurasian H9N2 (LPAI) avian influenza viruses

A Eurasian lineage of H9N2 (LPAI) viruses is currently widespread among poultry in some areas, and has become very diverse, with numerous reassortants, including some that share internal genes with H5N1 viruses.[194,243-247] H9N2 viruses have been detected in wild birds including some terrestrial species.[247-249]

H9N2 viruses have been found occasionally in pigs, and might sometimes cause clinical signs in this species.[192-195,250] They have also been detected in dogs,[35,43] and by serology in cats,[251] and infections can be reproduced experimentally in both dogs and cats, although virus replication may be limited.[252,253] Serological evidence of infection was found in performing macaques in Bangladesh, and in wild plateau pikas in China.[201,254] Pikas could be infected experimentally.[201] H9N2 variants may differ in their ability to replicate in mammals and/or cause disease.[245,246]

Host range of the zoonotic H7N9 avian influenza viruses

An H7N9 LPAI virus, which has recently caused serious human outbreaks in China, circulates there in poultry.[14,15,255-259] This virus acquired some of its genes from H9N2 viruses.[256,260] It has diversified considerably since its introduction, and regionally distinct lineages now exist.[261]

Among birds, infections have mainly been found in poultry (and in environmental samples from poultry markets, farms and similar sites), although this virus or its nucleic acids were also detected in two pigeons, an asymptomatic tree sparrow, and wild waterfowl.[259,262,263] Whether wild birds play any role in spreading this virus is uncertain.[259,263,264] Experimental infections have been established in Japanese quail (*Coturnix coturnix japonica*), several species of ducks, Embden geese, pigeons, zebra finches (*Taeniopygia guttata*), society finches (*Lonchura striata domestica*), house sparrows (*Passer domesticus*) and parakeets (*Melopsittacus undulates*), but pigeons and Pekin ducks were resistant to infection (requiring high doses), and only chickens and quail transmitted this virus efficiently to other birds.[265-267] Nevertheless, some of these birds (including passerine birds and parakeets), shed high titers in oropharyngeal secretions, and may be capable of infecting humans.[266]

There have been no reports of illnesses in mammals, as of November 2015, and no evidence of H7N9 infections was found among stray dogs living near live poultry markets.[35] In experimental studies, isolates from humans could infect miniature pigs, ferrets, laboratory mice and cynomolgus macaques.[268-270] At present, there have been no reports of infected pigs in China,[259] and one serological survey reported little or no evidence of exposure in this species.[271]

H7N7 LPAI viruses that resemble these H7N9 viruses in some of their genes have also been identified among poultry in China, and might have the potential to infect mammals.[260]

Other avian influenza viruses reported in mammals

Infections caused by other avian influenza viruses are reported sporadically in mammals. In addition to H5N1 and Eurasian H9N2 viruses, diverse subtypes (e.g., H4, H5N2, H5N6, H6N6, H7, H10N5 and H11N2) have been isolated occasionally from pigs, especially in Asia, and antibodies to avian H3 viruses have also been found.[39,98,192-194,196-200,271,272] While many infections with avian influenza viruses are transient, some established swine influenza viruses are wholly of avian origin or contain avian-origin gene segments.[45,46,55,57,192,193,250] (The Swine Influenza factsheet has additional information about these viruses.) One avian H3N8 virus affected horses in China for a short time, starting in 1989, but did not persist long term.[273,274] An H10N4 virus was responsible for an epidemic in farmed mink in Europe, and an H9N2 virus was recently isolated from this species in Asia.[31,203] Experimental infections with H3N8, H4N6, H5N3, H7N7, H8N4, H9N2 and H11N4 avian influenza viruses have been established in mink.[1,31,203,275]

Cats have been infected experimentally with some LPAI viruses (H1N9, H6N4, and H7N3) from waterfowl, as well as with an H7N7 HPAI virus isolated from a fatal human illness.[276-278] An H6N1 virus was isolated from a dog coinfected with canine distemper virus,[38] and dogs were also infected experimentally with an H6N1 LPAI virus.[279] In addition, serological evidence of infection with H10N8 viruses has been reported in dogs,[280] Domesticated guinea pigs in South America had antibodies to H5 influenza viruses.[281]

Few studies have investigated wild animals; however, antibodies to H4 and H10 viruses were found in raccoons in the U.S. (in addition to antibodies to H1 and H3 viruses, which could also originate from mammals), and antibodies to H3N8 viruses, possibly of avian origin, were reported in Japan.[230,282,283] Raccoons could be infected experimentally with an avian H4N8 virus,[282] striped skunks (*Mephitis mephitis*) with H4N6 and H3N8 viruses, and cottontail rabbits with an H4N6 virus,[284,285; 286 cited in 284] A number of influenza viruses (H3N3, H3N8, H7N7, H4N5, H4N6 and H10N7), closely related to avian viruses, have been isolated from seals.[1,31,202,287,288] Similarly, H1N3, H13N2 and H13N9 viruses, most likely of avian origin, have been isolated from whales.[1,31] Antibodies to various subtypes, some maintained only in birds, have also been detected in seals, and in some cases, in sea lions, walruses (*Odobenus rosmarus*) or porpoises.[31,287,289-291]

Laboratory mice (*Mus musculus*) and ferrets serve as models for mammalian infections with influenza viruses, including avian influenza viruses.[292-300] Most laboratory mice have a defective gene (Mx1), which increases their susceptibility to influenza viruses compared to their wild-type progenitors.[301-303] However, one recent study suggested that wild *Mus musculus* mice may also be susceptible to experimental inoculation with certain LPAI viruses.[301] Wild house mice (*Mus musculus*) at the site of an H5N8 avian influenza outbreak in poultry had serological evidence of infection with influenza A viruses (either avian or mammalian), but confirmatory testing and identification of the serotype could not be done due to the low sample volumes, and the virus could not be detected directly.[301] Some other studies have found no evidence for influenza viruses in wild mice.[304-306]

Zoonotic potential

The two most commonly reported avian influenza viruses from human clinical cases have been the Asian lineage H5N1 HPAI viruses, and recently, H7N9 LPAI viruses in China.[14,15,46,107,255-259,307] There have been no reported human infections caused by Asian lineage H5N8 viruses, although four infections with H5N6 viruses have been reported in China since 2014.[16,308-310] Illnesses caused by other subtypes have also been reported sporadically, with documented clinical cases caused by H9N2 (Eurasian lineage), H6N1 and multiple H7 and H10 avian influenza viruses.[100,107,287,311-331] Whether these infections are truly less common than subtypes such as H5N1 is unclear: viruses that tend to cause milder illnesses (e.g., H9N2 viruses) are less likely to be identified than those causing severe disease. Serological surveys in some highly exposed populations suggest the possibility of low level exposure to HA types found in birds, including H4, H5, H6, H7, H9, H10, H11 and H12.[194,323,332-347] Human volunteers were also infected with some subtypes (e.g., H4N8, H10N7 and H6N1), and sometimes developed mild respiratory signs and other influenza symptoms.[323] Adaptation to humans is possible, though rare, and some previous human pandemics were caused by partially or wholly avian viruses.[1,44-46,48,49,348]

Geographic Distribution

LPAI viruses are cosmopolitan in wild birds, although the specific viruses differ between regions.[1,7,93,95] These viruses are often absent from commercial poultry in developed nations, but they may be present in other domesticated birds.[3] Eurasian lineage H9N2 viruses are currently widespread among poultry in parts of Asia and the Middle East.[349-352] They have been detected in wild birds in Europe, where they also caused a few outbreaks in poultry flocks, and were isolated from game birds.[248,353,354] The zoonotic H7N9 LPAI viruses causing outbreaks in mainland China have not been reported from other regions, with the exception of imported cases in travelers.[14,15,355,356]

HPAI viruses are eradicated from all domesticated birds, whenever possible, and developed countries are usually HPAI-free. Asian lineage H5N1 HPAI viruses are currently considered to be endemic among poultry in a few nations in Asia and the Middle East, with outbreaks occurring at times in other countries in the Eastern Hemisphere.[12] These H5N1 viruses can also be found in wild birds in Eurasia,[27,142,144-147,149,225,226,357,358] but have not been detected in the Americas, Australia or New Zealand, as of 2015.[27,80-86,359,360] Asian lineage HPAI H5N8 viruses were widely detected in Asia and Europe in 2014, and reached North America (the Pacific Northwest region) in late 2014.[156,219,220] In North America, these viruses have reassorted with North American lineage viruses to generate unique viruses of other subtypes such as H5N1 and H5N2 (e.g., containing HA from the H5N8 virus and NA from a North American LPAI virus).[156,220] Whether the H5N8 viruses or any of these reassortants will persist in the Americas is still uncertain. Worldwide eradication of the Asian lineage H5 viruses is not expected in the near future.[12,361]

Transmission

Avian influenza viruses are shed in the feces and respiratory secretions of birds, although the relative amount of virus can vary with the specific virus, host species and other factors.[1,2,58,79,362,363] The feces contain large amounts of virus in aquatic birds such as waterfowl, and the fecal-oral route is thought to predominate in wild bird reservoirs.[7,149,364,365] Fecal-cloacal transmission might also be possible, but respiratory transmission is ordinarily thought to play little or no role.[7] However, there are some exceptions. Some viruses that have adapted to gallinaceous poultry, such as recent isolates of Asian lineage H5N1 HPAI viruses, can be found in higher quantities in respiratory secretions than the feces, even in wild waterfowl.[149,171,366,367] There are also reports of a few LPAI viruses found mainly in respiratory swabs from wild waterfowl,[368] and respiratory spread might be important in some wild terrestrial birds.[7,132]

Once an avian influenza virus has entered a poultry flock, it can spread on the farm by both the fecal–oral route and aerosols, due to the close proximity of the birds. Fomites can be important in transmission, and flies may act as mechanical vectors.[2,4,369,370] The possibility of wind-borne transmission of HPAI viruses between farms was suggested by one study,[371] but has not been conclusively demonstrated. Avian influenza viruses have also been found in the yolk and albumen of eggs from chickens, turkeys and quail infected with HPAI viruses.[372-378] Although infected eggs are unlikely to hatch, broken eggs could transmit the virus to other chicks in the incubator. It might be possible for LPAI viruses to be shed in eggs, but the current evidence suggests this is very rare, if it occurs at all.[372,379]

How long birds remain contagious differs between avian species, and with the severity of the infection (chickens and turkeys infected with HPAI viruses die very soon after infection). Most chickens usually excrete LPAI viruses for a week, and a minority of the flock for up to two weeks, but individual birds of some species, including waterfowl, can shed some LPAI or HPAI viruses for a few weeks in the laboratory.[46,131,167,380-382]

Transmission of avian influenza viruses to mammals

People and other mammals are usually infected with avian influenza viruses during close contact with infected birds or their tissues, although indirect contact via fomites or other means is also thought to be possible.[12,15,23,25,26,29,30,33,190,232,383-393] Respiratory transmission is likely to be an important route of exposure, and the eye may also act as an entry point.[269,298,300,394,395] A few H5N1 HPAI virus infections in animals, and rare cases in humans, have been linked to the ingestion of raw tissues from infected birds.[22,23,25,26,29,30,33,232,386,391,392] Housecats in an animal shelter might have become infected from contaminated avian feces, ingested while grooming.[190] Feeding experiments provide evidence that H5N1 viruses can enter the body by the oral route in cats, pigs, ferrets, mice, hamsters and foxes, and transmission has been confirmed in cats by direct inoculation of the virus into the gastrointestinal tract.[22,30,232,234,235,391,396,397] In humans, the strongest evidence for oral transmission is that two people became infected with an Asian lineage H5N1 virus after eating uncooked duck blood.[391] There are other human cases where ingestion probably occurred, but additional routes of exposure also existed.[392]

A ferret model suggested that some viruses might be transmitted to the fetus, when there is high viremia during systemic infections.[398] Viral antigens and nucleic acids were also found in the fetus of a woman who died of an Asian lineage H5N1 infection.[399] Transplacental transmission seems much less likely with influenza viruses that replicate only in the respiratory tract.

Host-to-host transmission of avian influenza viruses in mammals

Infected animals and people shed avian influenza viruses in respiratory secretions. Fecal shedding has been reported occasionally, although its significance is still uncertain.[400,401] Some avian influenza viruses that have been detected in feces include Asian lineage H5N1 HPAI viruses in humans and experimentally infected cats and foxes; H7N9 viruses in humans; and Eurasian H9N2 viruses in experimentally infected dogs.[29,234-238,252,402-405] Most studies used PCR, and the presence of live influenza viruses in feces was confirmed by virus isolation in only rare instances. The source of these viruses is still uncertain, and could be swallowed respiratory fluids, but Asian lineage HPAI H5N1 viruses seem to be able to replicate in human intestinal tissues.[406] There are also reports of Asian lineage H5N1 HPAI viruses in the urine of some mammals.[31]

Sustained transmission of avian influenza viruses is a rare event in mammals, but limited host-to-host transmission has caused clusters of infections or outbreaks in animals (e.g., in mink and horses).[1,31,192-194,198,287,288,407] While most infected people do not seem to transmit avian viruses to others, including family members,[311-313,316] Asian lineage H5N1 HPAI viruses are capable of person-to-person transmission in rare instances,[387-390] and one H7N7 HPAI virus was found in a few family members of poultry workers in the Netherlands.[316,408] Likewise, the H7N9 virus in China does not appear to spread readily between people, but human-to-human transmission was suspected in a few family clusters and one case of suspected nosocomial transmission in a hospital.[15,355,384,385,409-414] Close, unprotected contact, seems to be necessary to transmit any of these viruses.[387-390,412,413] Sometimes person-to-person transmission can be difficult to distinguish from exposure to a common source of the virus (e.g., on fomites).

Animal-to-animal transmission of Asian lineage H5N1 HPAI viruses was reported among tigers in one outbreak at a zoo, and experimentally between cats.[26,232,234] However, asymptomatic, naturally infected cats appeared to excrete these viruses only sporadically, and there was no evidence for animal-to-animal transmission.[190] In another study, there was no evidence for H5N1 virus transmission between small numbers of experimentally infected dogs and cats.[236] One experiment indicated that H5N1 viruses are not transmitted between pigs,[17] but recent evidence from Indonesia suggested that limited pig-to-pig transmission occurred within infected herds.[415] Some authors have also speculated about the possibility of virus transmission between mammals and birds in wild ecosystems, based on evidence from Qinghai Lake, China, where H5N1 viruses related to those previously found in wild plateau pikas[191] were isolated from dead migratory birds in 2009-2010, although this clade had not been found in wild aquatic birds at this location in 2007.[416] However, there was no serological evidence of exposure to H5 viruses in a recent study of plateau pikas in this area, despite evidence of exposure to H9 viruses.[201]

Survival of influenza viruses in the environment

Fecal-oral transmission of avian influenza viruses in birds may be facilitated by prolonged survival in some environments. The persistence of these viruses can be influenced by many factors such as the initial amount of virus; temperature and exposure to sunlight; the presence of organic material; pH and salinity (viruses in water); the relative humidity (on solid surfaces or in feces); and in some studies, by the viral strain.[380,417-431] Avian influenza viruses survive best in the environment at low temperatures, and some studies suggest that they are more persistent in fresh or brackish water than salt water.[380,381,417,418,420,422,424,426,427,431-434] Some viruses may survive for several weeks to several months or more in distilled water or sterilized environmental water, especially under cold conditions.[417,418,420-422] However, the presence of natural microbial flora may considerably reduce their survival in water, and at some temperatures, viruses may remain viable for only a few days (or less, in some environments) to a few weeks.[421-423,426,435] Other physical, chemical or biological factors in natural aquatic environments may also influence persistence.[421,422,434,435] Freeze-thaw cycles might help inactivate influenza viruses in cold climates.[425]

In feces, some anecdotal field observations stated that LPAI viruses can survive for at least 44 or 105 days, but the conditions were not specified.[417] Under controlled laboratory conditions, LPAI or HPAI virus persistence in feces ranged from < 1 day to 7 days at temperatures of 15-35°C (59-95°F), depending on the moisture content of the feces, protection from sunlight and other factors.[381,424,426,428,432,433,436] At 4°C (39°F), some viruses survived for at least 30-40 days in two studies,[426,432] but they remained viable for times ranging from less than 4 days to 13 days in two recent reports.[424,433] On various solid surfaces and protected from sunlight, viruses were reported to persist for at least 20 days and up to 32 days at 15-30°C (59-86°F);[381] and for at least 2 weeks at 4°C if the relative humidity was low;[424] but also for less than 2 days on porous surfaces (fabric or egg trays) or less than 6 days on nonporous surfaces at room temperature.[437] Survival was longer on feathers than other objects in two reports: at least 6 days at room temperature in one study,[437] and 15 days at 20°C (68°F) and 160 days at 4°C in another report.[433.] Some viruses persisted for up to 13 days in soil (4°C),[,424] for more than 50 days (20°C) or 6 months (4°C) in poultry meat (pH 7),[419] and for 15 days in allantoic fluid held at 37°C (99°F).[430] Exposure to direct sunlight greatly reduced virus survival.[424] Environmental sampling in Cambodia suggested that virus persistence in tropical environments might be brief: although RNA from Asian lineage H5N1 HPAI viruses was found in many samples including dust, mud, soil, straw and water, virus isolation was only successful from one water puddle.[438]

Disinfection

Influenza A viruses are susceptible to a wide variety of disinfectants including sodium hypochlorite, 60% to 95% ethanol, quaternary ammonium compounds, aldehydes (glutaraldehyde, formaldehyde), phenols, acids, povidone-iodine and other agents.[79,417,439-442] Influenza A viruses can also be inactivated by heat of 56-60°C (133-140°F) for a minimum of 60 minutes (or higher temperatures for shorter periods), as well as by ionizing radiation or extremes of pH (pH 1-3 or pH 10-14).[79,381,417,439,441]

Infections in Animals

Incubation Period

The incubation period in poultry can be a few hours to a few days in individual birds, and up to 2 weeks in the flock.[2,3,79] A 21-day incubation period, which takes into account the transmission dynamics of the virus, is used for an avian population in the context of disease control.[2] The incubation period for avian influenza viruses in mammals is also thought to be short, and might be as little as 1-2 days in some cases.[396]

Clinical Signs

Low pathogenic avian influenza

LPAI viruses usually cause subclinical infections or mild illnesses in poultry and other birds.[2,179,259,265,266] Decreased egg production, misshapen eggs, decreased fertility or hatchability of the eggs, respiratory signs (sneezing, coughing, ocular and nasal discharge, swollen infraorbital sinuses), lethargy, decreased feed and water consumption, or somewhat increased flock mortality rates may be seen in chickens and turkeys.[2,3,70,376,443-451] Illnesses exacerbated by factors such as concurrent infections or young age can be more severe.[3,58,179,452] Viruses with higher virulence might also exist. One unusual H10 virus isolated from waterfowl affected the kidneys and had a 50% mortality rate in some intranasally inoculated chickens.[64]

Some gallinaceous game birds (e.g., quail, pheasants, guinea fowl, partridges) infected with LPAI viruses have been asymptomatic, while others had clinical signs including lethargy, respiratory signs such as sinusitis, conjunctivitis, decreased egg production and diarrhea.[452] One study reported neurological signs and elevated mortality in guinea fowl (*Numida meleagris*) infected with an H7N1 virus.[452] High mortality has been seen in young ostriches in some outbreaks; however, a virus isolated from one outbreak caused only green diarrhea in experimentally infected young birds.[182] Domesticated waterfowl (e.g., ducks and geese) are often infected subclinically, although there may be mild signs such as sinusitis.[3,179]

Wild birds infected with LPAI viruses usually have few or no obvious clinical signs,[7,364] even during some epidemics among young birds at breeding colonies.[113,114,120; 115 cited in 114] However, subtle effects (e.g., decreased weight gain, behavioral effects or transient increases in body temperature) have been described in some cases.[84,453,454]

The H9N2 viruses currently circulating among poultry in the Eastern Hemisphere appear to be relatively virulent, and may cause significant respiratory signs and malaise in chickens, including experimentally infected birds that are not co-infected with other pathogens.[455,456] Both broilers and layers can be affected by these viruses.[352,455,456] Although quail are usually mildly affected by most other LPAI viruses, clinical signs were reported in some H9N2 outbreaks and experimentally infected birds.[352,455,457] One H9N2 virus caused severe clinical signs in experimentally infected quail, and mild signs in jungle fowl, while house sparrows developed respiratory signs, and crows (*Corvus splendens*) had mild or no signs.[455] The zoonotic H7N9 LPAI viruses in China have caused only mild or asymptomatic infections in poultry and experimentally infected birds including poultry, parakeets and most songbirds.[259,262,265,266] One house sparrow became ill with lethargy and loose droppings and died during this experiment, and one zebra finch died without clinical signs, but these deaths might not have been caused by the virus.

HPAI viruses in birds

HPAI viruses usually cause severe illness in chickens and turkeys, and few birds in infected flocks survive.[1,2,164] Marked depression, decreased feed and water intake, and other systemic, respiratory and/ or neurological signs are often seen, but no signs are pathognomonic, and sudden death can also occur.[2-4,10,58,79,164,165,169,376,458-461] Commonly reported signs include coughing, sneezing, sinusitis, blood-tinged oral and nasal discharges, ecchymoses on the shanks and feet, edema and cyanosis of the unfeathered skin on the head, comb and wattle (and snood in turkeys), and diarrhea. Egg production drops or ceases, and depigmented, deformed and shell-less eggs may be produced. Because a virus can be defined as highly pathogenic based on its genetic composition alone, HPAI viruses may rarely be found in chicken or turkey flocks that have mild signs consistent with low pathogenic avian influenza.[58,67]

HPAI virus infections can be asymptomatic, mild or severe in other birds, including gallinaceous birds other than chickens and turkeys.[1,2,7,27,32,58,79,126,139,141,143,144,146,148,149,151,152,164-167,179,182,186-188] Nonspecific clinical signs (e.g., anorexia, lethargy), neurological signs, diarrhea and sudden death have been reported in gallinaceous game birds, but milder or minimal signs were seen in some flocks.[165-167,452] Domesticated waterfowl tend to be mildly affected, but respiratory signs (e.g., sinusitis), diarrhea, corneal opacity, occasional cases with neurological signs, and increased mortality may be seen, and some Asian lineage H5N1 HPAI viruses can cause severe acute disease with neurological signs and high mortality rates.[2,79,145,146,148-150,171,172,462-464] Pigeons are also thought to be relatively resistant to illness, although there have been reports of sporadic deaths and rare outbreaks, with clinical signs that included neurological signs, greenish diarrhea and sudden death.[10,131,465] Some pigeons that were experimentally infected with H5N1 viruses remained asymptomatic, while others became moderately to severely ill.[10,131,465]

There is limited information about avian influenza viruses in ostriches, but HPAI viruses may not necessarily be more pathogenic than LPAI viruses in this species.[182,184-188] The clinical signs tend to be mild in adult ostriches, and more severe in young birds less than 6 months of age, which can develop nonspecific signs (e.g., depression), dyspnea; green urine, diarrhea or hemorrhagic diarrhea, with increased mortality.[182,187-189] Elevated mortality reported in some outbreaks in ostriches, pigeons and other relatively resistant birds might be caused by concurrent infections and other complications.[187,465]

Studies in experimentally infected wild birds and observations in captive and wild birds suggest that some species can be severely affected by Asian lineage H5N1 HPAI viruses, while others may have much milder signs or shed viruses asymptomatically.[32,126,143,144,146,148-152,172,227,466-468] During one H5N1 outbreak at a wildlife rescue center, some birds died without preceding clinical signs, while others developed anorexia, extreme lethargy, dark green diarrhea, respiratory distress and/or neurological signs, with death often occurring within 1-2 days.[32] Some species at the facility did not seem to be affected. Neurological signs, varying from mild to severe, have been documented in a number of experimentally infected wild birds including some species of ducks, geese, gulls, house finches and budgerigars, as well as in naturally or experimentally infected raptors.[148,151,172,227,469,470,470-474] Respiratory and nonspecific signs were reported in experimentally infected common reed buntings (*Emberiza schoeniclus*).[475] Other experimentally infected birds, such as zebra finches and brown-eared bulbuls (*Hypsipetes amaurotis*), had high mortality rates, but only nonspecific signs of depression and anorexia, or sudden death.[151] Starlings, pale thrushes (*Turdus pallidus*) and some species of ducks were mildly affected or unaffected, while house sparrows developed severe clinical signs in one study, and remained asymptomatic in another.[148,151,152,475]

Asian lineage H5N8 viruses have also been associated with wild bird die-offs in some countries, and these viruses and/or their reassortants have been detected in wild birds including sick, dead and apparently healthy waterfowl, and sick or dead birds in several other orders including raptors.[137,138,157,160-162,220,222,476] In some cases, the virus appeared to have affected the brain and the kidneys.[137] Experimental infections with one H5N8 isolate were asymptomatic in mallards, and either fatal or asymptomatic in Baikal teal (*Anas formosa*) [477]

Information about the effects of other HPAI viruses on wild birds is limited. Wild waterfowl infected with most viruses seem to be resistant to clinical signs,[10,140,149] but an H5N3 HPAI virus caused high mortality among South African terns in the 1960s.[139,141] A wild siskin naturally infected with an H7N1 HPAI virus was ill, and the same virus caused conjunctivitis, apathy and anorexia, with a high mortality rate, in captive canaries (*Serinus canarius*) that had been exposed to this bird.[141]

Mammals infected with Asian lineage H5N1 viruses

Asian lineage H5N1 HPAI viruses have caused fatal disease, as well as milder illnesses or asymptomatic infections, in mammals. A few clinical cases have been described, at most, in each species. Both symptomatic and subclinical infections have been reported in felids. One cat had a fever, depression, dyspnea, convulsions and ataxia, and a few infected housecats were found dead.[24,25,29] One of the latter cats was apparently well up to 24 hours before its death. Fatal illnesses with conjunctivitis and severe respiratory signs were described in experimentally infected cats.[232,234,236,396,478] Asymptomatic infections were reported in housecats in an animal shelter that had been accidentally exposed to a sick, H5N1-infected swan.[190] Some captive tigers and leopards died with clinical signs of respiratory distress, serosanguineous nasal discharge, high fever and neurological signs.[22,23,26,31,37] In another outbreak, captive lions, tigers, leopards and Asiatic golden cats were lethargic and had decreased appetites (without respiratory signs) for 5-7 days, but recovered.[32]

A dog that had eaten infected poultry developed a high fever, with panting and lethargy, and died the following day.[30] However, serological and virological evidence of infection has also been found in stray dogs in China during routine surveillance.[35] Most experimentally infected dogs remained asymptomatic or had relatively mild signs such as fever (which was transient in some studies), anorexia, conjunctivitis and/or diarrhea.[34,236,237] More severe respiratory signs (cough, labored breathing), with one fatal infection, were reported only in dogs inoculated directly into the trachea.[34] A study that infected both dogs and cats found that the cats were more susceptible and developed severe clinical signs, while the dogs were more likely to have few or no signs despite shedding virus.[478]

Experimental infections, as well as reports of infected herds, suggest that H5N1 HPAI virus-infected pigs usually remain asymptomatic or have only mild signs (e.g., mild respiratory disease and anorexia).[17,36,228,235,415] Fever, respiratory and/or neurological signs, as well as sudden death, have been reported in a handful of cases in other species.[20,31,33] One H5N1 virus was isolated from donkeys during a respiratory disease outbreak in Egypt, and a subsequent investigation detected antibodies to these viruses in healthy donkeys and horses in that country..[20,228] The role of the H5N1 virus in this outbreak was unclear, as the affected donkeys responded well to antibiotics. Fatal respiratory disease, and possibly diarrhea, was reported in H5N1 virus-infected raccoon dogs, while captive palm civets had neurological signs, with evidence of interstitial pneumonia, encephalitis and hepatitis at necropsy, and a wild stone marten was found with neurological signs.[31,33]

Mammals infected with other subtypes

Infections with influenza A viruses, apparently of avian origin, have been associated with outbreaks of pneumonia or mass mortality in seals.[1,100,202,479,480] The clinical signs in some outbreaks included weakness, incoordination, dyspnea and subcutaneous emphysema of the neck.[31,287,479] A white or bloody nasal discharge was seen in some animals. Experimental infections with these viruses were milder or asymptomatic, suggesting that co-infections may have increased the severity of the illness.[31] An influenza virus was also isolated from a diseased pilot whale, which had nonspecific signs including extreme emaciation, difficulty maneuvering and sloughing skin.[479] Whether this virus was the cause of the disease or an incidental finding is uncertain.[407] Other viruses were isolated from whales that had been hunted, and were not linked with illness.[481]

There are only a few reports of naturally acquired or experimental infections in other mammals, except in animal models for human disease (ferrets and mice). An H10N4 virus caused respiratory signs (sneezing, coughing, and nasal and ocular discharges) and elevated mortality in mink during an outbreak in Europe.[1,31] An H9N2 virus outbreak among mink in China was characterized by mild respiratory signs, with no reported deaths.[203] Respiratory signs were seen in a dog infected with an Asian lineage H5N2 HPAI virus in China, and this virus caused mild respiratory signs in experimentally infected dogs.[40,42] One cat exposed to these dogs developed respiratory signs and conjunctivitis, but 4 other cats seroconverted without clinical signs.[41] One study reported no clinical signs and inefficient virus replication in dogs that were experimentally infected with an Asian lineage H5N8 virus, while cats had mild and transient signs, including fever and marginal weight loss.[240]

Coughing, sneezing and nasal discharge were reported in dogs inoculated with a Eurasian H9N2 virus, and 13 H9N2 viruses were isolated from sick and healthy dogs in a study from China.[43,252] Some of the sick dogs in the latter study had clinical signs that could be consistent with influenza virus infections, but other infected dogs had signs likely to be unrelated.[43] Dogs and cats experimentally infected with an H9N2 virus remained asymptomatic, although virus replication was detected, especially in cats.[253] Few or no clinical signs were seen in cats inoculated with an H7N7 HPAI virus isolated from a fatal human case, cats inoculated with several LPAI viruses from waterfowl, or raccoons experimentally infected with an H4N8 virus.[276,277,282]

No natural infections with the zoonotic H7N9 LPAI viruses in China have been reported, as of November 2015, and experimental inoculation of this virus resulted in fever alone in cynomolgus macaques and asymptomatic infections in miniature pigs.[268]

Post Mortem Lesions [Click to view images]

Low pathogenic avian influenza in birds

Poultry infected with LPAI viruses may exhibit rhinitis, sinusitis, congestion and inflammation in the trachea, but lower respiratory tract lesions such as pneumonia usually occur only in birds with secondary bacterial infections.[2,3] Lesions (e.g., hemorrhagic ovary, involuted and degenerated ova) may also be observed in the reproductive tract of laying hens, and the presence of yolk in the abdominal cavity can cause air sacculitis and peritonitis.[2] A small number of birds may have signs of acute renal failure and visceral urate deposition.[3]

Highly pathogenic avian influenza in birds

The lesions in chickens and turkeys are highly variable and resemble those found in other systemic avian diseases.[462,482] Classically, they include edema and cyanosis of the head, wattle and comb; excess fluid (which may be blood-stained) in the nares and oral cavity; edema and diffuse subcutaneous hemorrhages on the feet and shanks; and petechiae on the viscera and sometimes in the muscles.[2,3,482] There may also be other abnormalities, including hemorrhages and/or congestion in various internal organs including the lungs, as well as severe airsacculitis and peritonitis (caused by yolk from ruptured ova).[2] However, the gross lesions in some outbreaks may not fit the classical pattern,[482] and birds that die peracutely may have few or no lesions.[2,3,482]

Variable lesions have also been reported in other gallinaceous birds.[452] Necrotic lesions in the pancreas (multiple foci of parenchymal discoloration) are common in quail and partridges infected with some HPAI viruses.[452] There may also be splenomegaly with parenchymal mottling, renal lesions, hemorrhages in internal organs and skeletal muscles, and pulmonary lesions (consolidation, edema, congestion and hemorrhages). However, some lesions seen in chickens and turkeys, such as cyanosis and hemorrhagic lesions in unfeathered skin, may not be as prominent in other gallinaceous birds.

In ostriches infected with avian influenza viruses, the gross lesions are usually hepatitis and peritonitis, with other secondary lesions.[187] Petechial hemorrhages, pancreatic lesions (e.g., multifocal hemorrhagic necrosis), pulmonary congestion and edema, and additional gross lesions have been reported in other species of birds infected with HPAI viruses.[144,148,151,227,483]

Avian H5N1 influenza viruses in mammals

Asian lineage H5N1 HPAI viruses can cause systemic lesions as well as pulmonary lesions in some animals. Gross lesions reported in some cats and other felids included pulmonary consolidation and/or edema, pneumonia; hemorrhagic lesions in various internal organs; and in some cases, other lesions such as multifocal hepatic necrosis, hemorrhagic pancreatitis, or cerebral, renal and splenic congestion.[23-25,29,232,234,396] Bloody nasal discharge, severe pulmonary congestion and edema, and congestion of the spleen, kidney and liver were reported in a naturally infected dog.[30] Pulmonary lesions including interstitial pneumonia have been noted in some experimentally infected pigs,[17] while others had mild to minimal gross lesions.[235]

Diagnostic Tests

Avian influenza viruses can be detected in oropharyngeal, tracheal and/or cloacal swabs from live birds, with differing recovery rates from each site depending on the virus, species of bird and other factors.[58,363] Very small (pediatric) swabs can be valuable in small birds, but feces can be substituted if cloacal samples are not practical (e.g., cannot be collected without harming the bird).[58] A recent study, which examined experimentally infected birds, suggested that immature feathers may also be a useful sample.[484] Samples from internal organs (e.g., trachea, lungs, air sacs, intestine, spleen, kidney, brain, liver and heart) are also tested in dead birds suspected of having HPAI.[2,58] Diagnostic tests should be validated for the species of bird, and some tests that are useful in chickens and turkeys may be less reliable in other avian species.[58,131,184]

Virus isolation can be performed in all species, and can be useful for virus characterization. Avian influenza viruses are isolated in embryonated eggs, and can be identified as influenza A viruses with agar gel immunodiffusion (AGID), antigen-detection ELISAs or other immunoassays, or by a molecular test such as RT-PCR.[3,58] They can be subtyped with specific antisera in hemagglutination and neuraminidase inhibition tests, by RT-PCR, or by sequence analysis of the viral HA and NA genes.[58] Genetic tests to identify characteristic patterns in the HA (at its cleavage site) and/or virulence tests in young chickens are used to distinguish LPAI viruses from HPAI viruses.[2,58]

RT-PCR assays can detect influenza viruses directly in clinical samples, and real-time RT-PCR is the diagnostic method of choice in many laboratories[2,58,485] Viral antigens can be detected with ELISAs including rapid tests.[58,485] Currently, the World Organization for Animal Health (OIE) recommends that antigen detection tests be used to identify avian influenza only in flocks and not in individual birds.[58]

Serology can be valuable for surveillance and demonstrating freedom from infection, but it is not very useful in diagnosing HPAI infections in highly susceptible birds, as they usually die before developing antibodies.[58] Serological tests used in poultry include AGID, hemagglutination inhibition (HI) and ELISAs.[58] AGID tests and ELISAs to detect conserved influenza virus proteins can recognize all avian influenza subtypes, but HI tests are subtype specific and may miss some infections. Cross-reactivity between influenza viruses can be an issue in serological tests. Tests that can distinguish infected from vaccinated birds (DIVA tests) should be used in surveillance when vaccination is part of a control program.[58,72,486]

Treatment

There is no specific treatment for influenza virus infections in animals. Poultry flocks infected with HPAI viruses are depopulated (this is generally mandatory in HPAI-free countries), while the disposition of infected LPAI flocks may differ, depending on the specific virus and the country.

Control

Disease reporting

A quick response is vital for containing avian influenza outbreaks, and in some cases, for minimizing the risk of zoonotic transmission. In addition to national notification requirements, HPAI viruses and LPAI viruses that contain H5 or H7 must be reported to the OIE by member nations.[487] Veterinarians who encounter or suspect a reportable disease should follow their country-specific guidelines for informing the proper authorities (state or federal veterinary authorities in the U.S. for diseases in animals). Unusual mortality among wild birds should also be reported (e.g., to state, tribal or federal natural resource agencies in the U.S.[488])

Prevention

The risk of introducing a virus to poultry or other birds can be reduced by good biosecurity and hygiene, which includes preventing any contact with other domesticated or wild birds, mechanical vectors and fomites including water sources.[4,5,46,79,462] All-in/ all-out flock management is helpful in poultry flocks, and birds should not be returned to the farm from live bird markets or other slaughter channels.[4] To help prevent reassortment between human and avian influenza viruses, people are encouraged to avoid contact with birds while suffering flu symptoms.[45]

Avian influenza vaccines may include both inactivated whole virus vaccines and newer recombinant vectored vaccines.[489-491] Most vaccines are produced for chickens, although they may be validated for use in turkeys, and their effectiveness can differ in other species.[167,492] In addition to suppressing clinical signs, some vaccines are capable of increasing resistance to infection, and decreasing virus excretion and transmission.[145,167,176,177,362,493-503] However, clinical protection is not necessarily correlated with reduced virus shedding, and some birds can become infected even in the best case scenario.[178,504-506] Thus, vaccination can mask infections if good surveillance programs are not used simultaneously.[2,496,507,508] Vaccination can also place selection pressures on influenza viruses, which may encourage the emergence of vaccine-resistant isolates.[504,506,509,510] In different countries, vaccines may be used routinely to protect poultry flocks, as an adjunct control measure during an outbreak, or to protect valuable species such as zoo birds from highly virulent viruses such as H5N1.[58,287,507] Vaccination in the U.S. is restricted and requires the approval of the state veterinarian, and in the case of H5 and H7 vaccines, USDA approval.

During outbreaks, HPAI viruses are normally eradicated by depopulation of infected flocks, combined with other measures such as movement controls, quarantines and perhaps vaccination.[462] Insect and rodent control, disposal of contaminated material, and thorough cleaning and disinfection are also important.

For mammals, prevention involves avoiding close contact with infected birds or their tissues. Keeping susceptible animals indoors may be helpful during outbreaks.

Morbidity and Mortality

Birds

Exposure to influenza viruses and shedding patterns among wild birds are complex and likely to reflect their exposure to different habitats, as well as gregariousness and other social factors, and pre-existing immunity.[9,112] Reported infection rates with LPAI viruses range from <1% to more than 40%, and seroprevalence rates from <1% to greater than 95%, typically with much higher rates in birds from aquatic environments than terrestrial species.[8,9,84,89,109-112,114,118,127,128,133,134,511-514] Some studies have reported that infection rates are higher in young birds than adults (e.g., young egrets and herons at breeding colonies or young ducks).[84,109,113-115] LPAI virus prevalence can also be higher during certain seasons, such as in late summer staging areas before migration, when bird densities are high and young "hatch year" birds have not yet developed immunity.[515] Currently, surveillance suggests that carriage of H5N1 HPAI viruses in wild bird populations without unusual mortality events is rare.[226,357]

The prevalence of influenza viruses in poultry differs between nations, but commercial poultry in developed countries are often free of both LPAI and HPAI viruses.[3] Even in these regions, LPAI viruses may be present in backyard flocks, live poultry markets and similar sources.[3] HPAI outbreaks are uncommon under ordinary conditions, while LPAI outbreaks tend to occur more often. However, the continued presence of Asian lineage H5 HPAI viruses in poultry elevates the risk of outbreaks throughout the world. These H5N1 viruses tend to reemerge during colder seasons in endemic areas.[516,517]

Avian influenza differs in severity, depending on the species of bird as well as the virus. LPAI viruses usually cause mild illnesses or asymptomatic infections in birds, including chickens and ducks, but outbreaks can be more severe when there are concurrent infections or other exacerbating factors.[2,58,179] High mortality is occasionally seen in young ostriches infected with either LPAI or HPAI viruses, although adult birds seem to be only mildly affected by both.[10,182,184-188]

HPAI viruses usually cause high and rapidly escalating mortality in chicken and turkey flocks, with cumulative morbidity and mortality rates that may approach 90-100%.[2,12] Any survivors are usually in poor condition and do not begin laying again for several weeks. Morbidity and mortality rates can sometimes approach 100% in other domesticated and wild birds, but susceptibility can vary greatly, and certain species such as waterfowl tend not to be severely affected.[32,131,148,151,152,164-170,174,452,475] Some Asian lineage H5N1 viruses cause severe illness even in waterfowl, and the introduction of these viruses may be heralded by unusual deaths among wild birds (e.g., swans in Europe and recently crows in Pakistan).[1,32,46,143,144,146,149,153,357,358,462] Thousands of wild birds were killed in some outbreaks, such as one at Qinghai Lake, China in 2005.[518] Wild bird deaths have also been associated with some Asian lineage H5 reassortants, such as H5N8 viruses, in Asia.[137,138,157,160-162,220,222,476]

Mammals

Pigs seem to be infected fairly regularly by avian influenza viruses from birds, often with only minor consequences even when the virus belongs to the Asian lineage of H5N1 HPAI viruses.[1,5,17,19,36,39,46,98,150,192-194,196-200,415] Low levels of exposure have been reported for H5N1, H9N2 and other subtypes in some endemic areas, with seroprevalence to these viruses typically ranging from < 1% to 5% and occasionally higher, and virus detection rates of <1% to 7.5% in pigs during H5N1 outbreaks among poultry.[17,36,98,192-194,196-200,228,271,272,415,519] Some studies reporting higher seroprevalence to H5N1 viruses examined pigs in poor neighborhoods where they are fed dead bird carcasses and other organic remains, and in one Egyptian study, 8 of 11 positive samples came from a single herd.[36]

H5N1 HPAI virus infections reported in housecats and large zoo felids ranged from asymptomatic to fatal, while experimentally infected cats exhibited severe disease with high mortality.[23-26,29,31,32,37,190,232,234,478]. No seropositive cats were found in parts of Austria and Germany where these viruses had been found in wild birds, but low titers were detected in 8% of 25 cats in Egypt, and 73% of 11 cats in an unpublished study from Thailand.[18,228,520] Recently, a survey of more than 900 healthy cats in northeastern China reported that approximately 2% had antibodies to H5N1 viruses, using the HI test, but no sera reacted in a confirmatory microneutralization assay.[521] Another large survey, which examined 700 stray cats, found that a very small number of sera (3 cats) reacted to H5N1 viruses in both serological assays, and larger numbers of cats (18) had antibodies to H9N2 viruses.[251] Several avian influenza viruses have been reported in dogs, although in some cases, there may be little information about the consequences of infection. While there is one report of a fatal H5N1 HPAI case in a dog, experimental infections have been mild or symptomatic in this species, except when the inoculation method bypassed normal upper respiratory defense mechanisms.[30,34,236,237,478] Surveys reported antibodies to H5N1 viruses in 25% of dogs during outbreaks in Thailand, 4% of 25 dogs in Egypt (low titers), and 1% of stray dogs in live markets and on poultry farms in China, with virological confirmation of infection from 2 dogs in China by PCR.[18,35,228] Eurasian lineage H9N2 viruses have also been isolated from dogs,[43] and surveys in China reported seroprevalence rates to these viruses that ranged from <5% (with evidence of infection in 0.4% of dogs by RT-PCR) to 20-45% in various populations of dogs.[35,43] Unpublished work found serological evidence of exposure to H10N8 viruses in few feral dogs living near poultry markets, but whether this virus can affect dogs is not known.[280]

The effects of Asian lineage H5N1 HPAI viruses on equids are still uncertain, but some surveys from Egypt reported that approximately 25% of donkeys and horses were seropositive.[20,228] Fatal infections with these viruses have also been reported occasionally in other species such as raccoon dogs, palm civets and mink, but little more is known.[27,28,31,33] An outbreak caused by a avian H10N4 virus in 1984 affected 33 mink farms in Sweden, with a morbidity rate of nearly 100% and mortality rate of 3%.[1,31] However, an H9N2 outbreak among mink in China was reported to be mild, with no elevated mortality.[203] The prevalence of this virus in mink is currently uncertain; however, mink on some other Chinese farms were also seropositive.[203,275] The severity of influenza in mink is thought to be influenced by co-infections and other factors.[1,31,99,103,522,523]

Infections in Humans

Incubation Period

Most zoonotic infections caused by Asian lineage H5N1 HPAI viruses seem to become apparent within approximately 5 days, although the incubation period for some cases may be as long as 8 and possibly 17 days.[204,208] Estimates of the mean incubation period for the zoonotic H7N9 viruses have varied from 3 days (in two analyses, which considered large numbers of cases) to 5-6 days, with a range of 1-13 days.[384,410,411,524,525]

Clinical Signs

Asian lineage H5N1 HPAI viruses

Most infections with Asian lineage H5N1 HPAI viruses have been severe.[12,107,323] The initial signs are often a high fever and upper respiratory signs resembling human seasonal influenza, but some patients may also have mucosal bleeding, or gastrointestinal signs such as diarrhea, vomiting and abdominal pain.[204,208,526] Respiratory signs are not always present at diagnosis; two patients from Vietnam had acute encephalitis without symptoms to indicate respiratory involvement.[527] Similarly, a patient from Thailand initially exhibited only fever and diarrhea.[527] Lower respiratory signs (e.g., chest pain, dyspnea, tachypnea) often develop soon after the onset of the illness.[204,208] Respiratory secretions and sputum are sometimes blood-tinged.[204] Most patients deteriorate rapidly, and serious complications including heart failure, kidney disease, encephalitis and multiorgan dysfunction are common in the later stages.[204,208,526] Milder cases have been reported occasionally, particularly among children.[323,528]

Three infections with Asian lineage H5N6 HPAI viruses in older adults were also severe, with fever and severe respiratory signs in at least two patients.[308-310] One of these cases was fatal; the other patient required mechanical ventilation but recovered after treatment with oseltamivir and antibiotics (details of the third case have not been published).[309,310] A child infected with an H5N6 virus had a mild illness with prompt recovery.[308-310]

Eurasian lineage H9N2 LPAI viruses

Most illnesses caused by H9N2 viruses have been reported in children and infants.[107,323-329] These cases were usually mild and very similar to human influenza, with upper respiratory signs, fever, and in some cases, gastrointestinal signs (mainly vomiting and abdominal pain) and mild dehydration.[107,323-329] All of these patients, including a 3-month-old infant with acute lymphoblastic lymphoma,[329] made an uneventful recovery. Acute, influenza-like upper respiratory signs were also reported in two adults, a 35-year-old woman and a 75-year-old man.[325] Severe lower respiratory disease, which developed into respiratory failure, was seen in a 47-year-old woman, who had chronic graft vs. host disease and bronchiolitis obliterans after a bone marrow transplant, and was receiving immunosuppressive therapy.[329] She survived after treatment with antiviral drugs, antibiotics for pneumonia, and supportive care, but required long-term oxygen supplementation on discharge.

Zoonotic H7N9 LPAI viruses in China, 2013-2014

Most clinical cases caused by H7N9 viruses in China have been serious, to date.[14,15,255,404,529,530] The most common symptoms were fever and coughing, but a significant number of patients also had dyspnea and/or hemoptysis, and severe pneumonia (frequently complicated by acute respiratory distress syndrome and multiorgan dysfunction) developed in most laboratory-confirmed cases.[405,524,531] A minority of patients had diarrhea and vomiting, but nasal congestion and rhinorrhea were not common initial signs.[524,532] Conjunctivitis (which is a common sign with some other avian influenza viruses) and encephalitis were uncommon.[532] In most cases, patients deteriorated rapidly after the initial signs.[524,532] Concurrent bacterial infections were identified in some patients, and may have contributed to the clinical picture.[405,524]

A few uncomplicated cases were characterized by mild upper respiratory signs or fever alone, especially in children.[255,410,524,530,532,533] At least one asymptomatic infection has been reported in an adult.[404,524]

Other avian influenza viruses

Mild illnesses, with conjunctivitis and/or upper respiratory signs, have been reported in a number of people infected with various H7 LPAI or HPAI viruses and an H10N7 virus.[100,287,314-322,331] One H7N7 HPAI virus, which caused only mild illnesses in most people, resulted in fatal acute respiratory distress syndrome and other complications in one otherwise healthy person.[316] His initial symptoms included a persistent high fever and headache, but no signs of respiratory disease. The virus isolated from this case had accumulated a significant number of mutations, while viruses from most other infected individuals had not, and it also caused severe illness in experimentally infected ferrets and mice.[300,316] Severe illness (pneumonia) was reported in a person infected with an LPAI H7N2 virus; however, he had serious underlying medical conditions, including HIV infection and infection with *Mycobacterium avium* complex.[313] This patient was hospitalized but recovered without antiviral treatment. A 20-year-old woman infected with an H6N1 virus in China developed a persistent high fever and cough, progressing to shortness of breath, with radiological evidence of lower respiratory tract disease.[312] She made an uneventful recovery after treatment with oseltamivir and antibiotics. Severe lower respiratory tract disease, progressing in some cases to multiple organ failure and septic shock, was reported in three people with H10N8 infections in China.[311,330] Two cases were fatal, one in a 73-year-old patient who had underlying health conditions, and another in a 75-year old. The third patient, who was 55 years of age, recovered after mechanical ventilation and treatment with various drugs including oseltamivir. The other two patients also received oseltamivir.

Diagnostic Tests

Avian influenza viruses may be detected in samples from the upper and/or lower respiratory tract, depending on the site of the infection.[12,208,259] RT-PCR is usually the primary test for Asian lineage H5N1 HPAI viruses.[208] RT-PCR assays have also been published for the H7N9 influenza viruses causing outbreaks in China.[410,534,535] Virus isolation can be performed, but it is slower.[536,537] Antiviral resistance can be evaluated with phenotypic tests or gene-based testing to detect molecular markers of resistance, but is available in a limited number of laboratories, and takes several days to perform.[537] Testing for novel influenza viruses is generally performed by state, regional or national public health laboratories, and in some cases by reference laboratories capable of handling dangerous human pathogens such as H5N1 HPAI viruses.[12,208]

During routine influenza diagnosis, testing that identifies the presence of influenza A, but does not detect the hemagglutinins in common human influenza viruses, might indicate a novel, possibly zoonotic, virus.[12] Commercial rapid diagnostic test kits used for seasonal human influenza virus infections may not detect avian influenza viruses.[12,536-541]

Serology is used for epidemiological studies, and occasionally for retrospective diagnosis of a case.[383] The microneutralization assay is considered to be the most reliable test for detecting antibodies to avian influenza viruses in humans,[208,323] although other serological tests (e.g. hemagglutination inhibition) have also been used.[537,542] No seroconversion occurred with some avian influenza viruses, even in virologically confirmed cases.[319,322] Seroconversion might also vary with the severity of the illness (and the test): although adults with severe illnesses caused by the H7N9 virus in China seroconverted, titers were low or absent in a few mild cases in children.[543]

Treatment

Treatment for avian influenza may vary, depending on the severity of the case. In addition to symptomatic treatment, it can include various drugs, including antibiotics to treat or prevent secondary bacterial pneumonia, and antivirals.[544,545] Two groups of antiviral drugs – the adamantanes (amantadine, rimantadine), and neuraminidase inhibitors (zanamivir, oseltamivir, peramivir and laninamivir) – are effective against some influenza A viruses, but some of these drugs (peramivir and laninamivir) are not licensed in all countries.[78,440,]

[536,541,546-549] Antiviral drugs are most effective if they are started within the first 48 hours after the clinical signs begin, although they may also be used in severe or high risk cases first seen after this time.[440,536,541,546-549] Oseltamivir appears to increase the chance of survival in patients infected with Asian lineage H5N1 and H7N9 viruses, particularly if it is given early.[208,526,527,550,551] Side effects including gastrointestinal and CNS effects are possible, particularly with some drugs.[536,541]

Antiviral resistance can develop rapidly in influenza viruses, and may even emerge during treatment.[1,78,541,552] At present, Asian lineage H5N1 HPAI viruses are usually sensitive to oseltamivir, and they are often (though not always) resistant to adamantanes.[12,208,516,553] Although resistance to zanamivir and oseltamivir has been reported, it is currently uncommon.[12,208,516,553] Likewise, the H7N9 LPAI viruses are often sensitive to oseltamivir, and all of the H7N9 isolates from humans have contained a mutation suggesting resistance to adamantanes.[256,355,531] Oseltamivir-resistant viruses of H7N9 viruses have also been described.[355,531] One recent study documented low levels of resistance to neuraminidase inhibitors among avian influenza viruses in wild birds.[554]

Prevention

Protective measures for zoonotic avian influenza viruses include controlling the source of the virus (e.g., eradicating HPAI viruses, closing infected poultry markets); avoiding contact with sick animals, animals known to be infected, and their environments; employing good sanitation and hygiene (e.g., hand washing); and using personal protective equipment (PPE) where appropriate.[12,204,385] While the recommended PPE can vary with the situation and risk of illness, it may include respiratory and eye protection such as respirators and goggles, as well as protective clothing including gloves.[12,488,555] The hands should be washed with soap and water before eating, drinking, smoking, or rubbing the eyes.[488]

Because HPAI viruses have been found in meat and/or eggs from several avian species,[71,177,372-378,445,556-560] careful food handling practices are important when working with raw poultry or wild game bird products in endemic areas, and all poultry products should be completely cooked before eating.[12,488,561] Sanitary precautions and cooking methods recommended to destroy *Salmonella* and other poultry pathogens in meat are sufficient to kill avian influenza viruses,[12] and eggs should be cooked until the whites and yolks are both firm.[12,488] Wild birds should be observed from a distance, as they may be infected with some viruses, and hunters should not handle or eat sick game.[488] H5N1 vaccines for humans have been developed in the event of an epidemic, but are not in routine use.[12,562]

More detailed recommendations for specific groups at risk of exposure (e.g., people who cull infected birds, field biologists, and hunters) have been published by some national agencies, including the CDC, the Department of the Interior and U.S. Geological Survey National Wildlife Health Center in the U.S.,[12,488,555,563] and international agencies such as the World Health Organization. In some cases, recommendations may include antiviral prophylaxis (e.g., for people who cull birds infected with Asian lineage H5N1 HPAI viruses) and/or vaccination for human influenza to reduce the risk of reassortment between human and animal influenza viruses.[12,45,527] People who become ill should inform their physician of any exposure to avian influenza viruses.

Morbidity and Mortality

H5N1 avian influenza

Between 1997 and September 2015, there were nearly 850 laboratory-confirmed human infections with Asian lineage H5N1 viruses, which generally occurred as the result of close contact with poultry.[16] Illnesses caused by H5N1 viruses have been rare, overall; however, these viruses have been found in poultry (including small backyard flocks) for over a decade, resulting in high levels of human exposure. Increased numbers of human infections have been noted recently in Egypt, possibly due to the prevalence of certain viral strains.[564] Most patients with illnesses caused by H5N1 viruses have been young and had no predisposing conditions.[208] The case fatality rate for all laboratory confirmed cases reported to WHO has consistently been about 59-60% in the last few years.[13,16,307] Likewise, a summary of confirmed, probable and suspected H5N1 cases documented worldwide between 2006 and 2010 found that 56% of these cases were fatal.[565] However, the case fatality rate differs between countries and groups of patients.[526,565-569] It is lower in young children than adults,[565,569,570] and in patients with milder symptoms at the time of diagnosis.[570] One study found that rhinorrhea was linked to improved survival, possibly because it was indicative of milder cases or upper respiratory disease.[569] Conversely, delays in antiviral (oseltamivir) treatment were associated with a worse prognosis.[569] The case fatality rate seems to be particularly low in Egypt, where 28% of confirmed, suspect and probable cases were fatal between 2006 and 2010, and the median age of patients was 6 years.[565] Their young age, which tends to be associated with early diagnosis, as well as treatment-related factors and the virulence of the circulating viruses might be factors in the relatively high survival rate.[565,569,570]

Antibodies to H5N1 viruses have been reported in some poultry-exposed populations that have no history of severe H5N1 disease, fueling speculation on the likelihood of asymptomatic or mild infections.[228,333,334,337,346,571-573] Most studies have reported seroprevalence rates of 0% to 5%, with a few reporting higher levels, and a meta-analysis of studies published before 2012 suggests that the overall seroprevalence is approximately 1-2% or less.[228,333,334,337,338,345,346,571-574] Factors such as cross-reactivity with human influenza viruses in serological assays, or poor seroconversion to some avian viruses, might influence estimates of exposure, and the true prevalence of mild cases is still uncertain and controversial. Rare, laboratory confirmed, asymptomatic or mild cases have also been recognized.[323,528,575] Rapid treatment with antiviral drugs might have been a factor in some of these cases; however, one child had only upper respiratory signs and made an uncomplicated recovery after antibiotic treatment alone.[528,565,569,570] Prospective studies from Nigeria and rural Thailand documented rare instances of seroconversion to H5 avian influenza viruses, but were unable to find virological evidence of any avian influenza viruses during influenza-like illnesses.[332,334,336] The occurrence of milder cases would be expected to lower the case fatality rate. However, it is possible that some severe cases have also been missed or attributed to other diseases; thus, the net effect of any undiagnosed cases is uncertain.

Three illnesses caused by Asian lineage H5N6 viruses in patients aged 49 years or older were severe; however, one infection in a child was mild.[308-310] One of the two published cases in older adults was fatal; the other person recovered with intensive treatment.[308,309]

H7N9 avian influenza

Approximately 680 laboratory-confirmed clinical cases, with at least 275 fatalities, have been caused by LPAI H7N9 viruses in China (or in travelers to China), as of September 2015.[16] They mainly occurred in three waves to date, the first consisting of approximately 130 cases between February and May 2013, the second from October 2013 to May 2014, and the third beginning in Fall 2015, with sporadic cases reported between outbreaks.[14,15,255,256,258,576] This H7N9 virus is circulating subclinically in poultry, and human illnesses have mainly been associated with live bird poultry markets, although infected farms have also resulted in at least one human illness.[15,259,383-385,576-579] During the first wave, culling of live birds in wholesale markets, and closure of markets with cleaning and disinfection, were associated with declines in the number of human cases.[385] However, many live markets were not closed, or re-opened after being closed for a short period.[256] Significant environmental contamination with H7N9 viruses has since been reported in some new poultry slaughter and processing plants, which have replaced live bird markets or serve as an alternative in some areas.[576]

Many of the clinical cases have occurred in older patients.[529] During the first wave, 55% of the patients were older than 59 years.[384] Elderly men were overrepresented in urban areas, particularly in locations where their traditional family roles result in increased exposure to retail live poultry, but men were not affected significantly more often than women in rural regions.[384,580] Most reported cases in adults (including young and middle-aged adults) have been serious, while many cases in children were mild.[15,255,259,404,524,529,530] Some cases may have been mitigated by prompt treatment with oseltamivir, but other mild cases occurred in people admitted to the hospital for observation alone, or were identified only after the person had recovered.[255,524,530,533] Analyses of cases to October, 2014 reported case fatality rates in hospitalized, laboratory confirmed patients of approximately 36% to 48% during the first two waves,[15,255,259,581] with the risk of death among hospitalized patients increasing significantly with age.[255,581] Concurrent diseases or predisposing causes have been reported in a significant number of patients (e.g., 45% of cases in the first wave), although serious cases and fatalities also occurred in previously healthy individuals.[255,259,356,384,404,410,524,529,582] Delayed treatment with antiviral drugs was also suggested as a possible factor in the high case fatality rate.[524,532]

The likelihood of additional, undiagnosed mild or asymptomatic infections is still being assessed. In the majority of cases, there was no virological evidence of exposure among patient contacts who developed influenza-like signs. Some of the known mild cases were identified through national virological sampling of people with influenza-like illnesses.[255,259,530] However, these samples are collected from people who visit primary care centers with influenza-like illnesses, and some cases could have been missed.[530] Some initial serological studies found no H7N9 reactivity among poultry market workers, healthcare staff, patient contacts and other populations.[256,409,411,583-585] However, several surveys have now detected antibody titers to H7N9 viruses in up to 17% of poultry workers or live bird market workers, with two studies documenting recent increases in seroprevalence.[576,586-588] These studies report that seroprevalence rates are low (≤ 1%) in the general population, [586,587] with one survey also documenting low seroprevalence in veterinarians. (2%).[588] Although cross-reactivity with other H7 viruses that may circulate in poultry is possible, these surveys suggest that mild or asymptomatic infections may have occurred among poultry workers. As a result, some authors have suggested that the overall case fatality rate in all symptomatic cases might be as low as <1% to 3%, if milder cases are also accounted for; however, such estimates currently have a high degree of uncertainty.[255,581]

H9N2 avian influenza viruses

Clinical cases caused by Eurasian lineage H9N2 viruses have mainly been reported in children.[12,16,107,194,323-328] Most cases, including an infection in an immunocompromised infant, have been mild, and were followed by uneventful recovery. Severe illness was reported in an adult with serious underlying medical conditions.[329] Many serological studies have found antibodies to H9N2 viruses in <1% to 5% of poultry-exposed groups in endemic regions; however, a few studies have reported higher seroprevalence rates, including 9% of agricultural workers in Bulgaria, 11% of poultry workers and 23% of live bird market workers in China, and 48% of poultry workers in Pakistan.[194,332-335,337,338,341,343,588-590] A review and meta-analysis of the literature, which included exposure to all H9N2 viruses worldwide in both

Eastern and Western Hemispheres, reported a median seroprevalence of 5%, using the HI test.[591] For microneutralization assays, the median seroprevalence rate was 3% (range <1% to 9%) if the cutoffs employed by the authors of each study were used, and 0.3% (range 0.1% to 1.4%) if these cutoffs were adjusted to those recommended by the World Health Organization. A prospective study of adults with poultry exposure in rural Thailand reported rare instances of seroconversion to H9 viruses, but the two people who seroconverted did not report being ill, and no avian influenza viruses were detected in other people who had influenza-like illnesses.[332]

Other avian influenza viruses

With the exception of the H7N9 viruses in China, most reported infections with H7 viruses in healthy people have been mild, whether they were caused by an LPAI or HPAI virus; however, one H7N7 HPAI virus caused a fatal illness in a healthy person, while affecting others only mildly.[100,287,314-321] Mild signs were reported in poultry workers infected with an H10N7 virus in Australia,[322] but H10N8 viruses caused fatal infections in two elderly patients in China and a serious illness in a 55-year-old.[311,330] A young woman infected with an H6N1 virus in China had evidence of lower respiratory tract complications, but recovered with treatment.[311,312] The possibility of other, unrecognized infections may be suggested by the occurrence of antibodies to various subtypes, generally at a low prevalence, in people who are exposed to poultry or waterfowl.[194,323,332,334,339-347,590,592-595] Susceptibility (and/or seroconversion) might differ between viruses: 3.8% of poultry workers seroconverted during an H7N3 LPAI outbreak in Italy in 2003, but no seropositive individuals were identified in serum samples collected during H7N1 epidemics from 1999-2002.[593] Rare seroconversion to H6, H7 and H12 viruses was reported in prospective studies of adults with poultry exposure in Cambodia and rural Thailand, but no clinical cases were identified.[332,347]

Internet Resources

Canadian Food Inspection Agency [CFIA]. Fact Sheet - Avian Influenza
http://www.inspection.gc.ca/animals/terrestrial-animals/diseases/reportable/ai/fact-sheet/eng/1356193731667/1356193918453

CFIA Notifiable Avian Influenza Hazard Specific Plan
http://www.inspection.gc.ca/animals/terrestrial-animals/diseases/reportable/ai/hazard-specific-plan/eng/1374504359532/1374504482294

Centers for Disease Control and Prevention. Avian Influenza
http://www.cdc.gov/flu/avianflu/

Department of the Interior. Appendix H: Employee Health and Safety Guidance for Avian Influenza Surveillance and Control Activities in Wild Bird Populations
http://www.doi.gov/emergency/pandemicflu/appendix-h.cfm

Public Health Agency of Canada (PHAC). Influenza
http://www.phac-aspc.gc.ca/influenza/index-eng.php

PHAC. Pathogen Safety Data Sheets
http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php

The Merck Manual
http://www.merckmanuals.com/professional/index.html

The Merck Veterinary Manual
http://www.merckmanuals.com/vet/index.html

United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS).
http://www.aphis.usda.gov/wps/portal/aphis/home/

USDA APHIS. Biosecurity for the Birds
http://www.aphis.usda.gov/animal_health/birdbiosecurity/

United States Geological Survey (USGS). National Wildlife Health Center. List of species affected by H5N1 (avian influenza)
http://www.nwhc.usgs.gov/disease_information/avian_influenza/affected_species_chart.jsp

USGS National Wildlife Health Center. Wildlife Health Bulletin #05-03 (with recommendations for field biologists, hunters and others regarding contact with wild birds)
http://www.nwhc.usgs.gov/publications/wildlife_health_bulletins/WHB_05_03.jsp

World Health Organization. Zoonotic Influenza
http://www.who.int/influenza/human_animal_interface/en/

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

OIE Terrestrial Animal Health Code
http://www.oie.int/international-standard-setting/terrestrial-code/access-online/

References

1. Acha PN, Szyfres B (Pan American Health Organization 309). Zoonoses and communicable diseases common to man and animals. Volume 2. Chlamydiosis, rickettsioses and virosis. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Influenza; p. 155-72.
2. Swayne DE. Avian influenza. In: Foreign animal diseases. Boca Raton, FL: United States Animal Health Association; 2008. p. 137-46.

3. Swayne DE. Overview of avian influenza. In: Aiello SE, Moses MA, editors. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2012. Available at: http://www.merckmanuals.com/vet/poultry/avian_influenza/overview_of_avian_influenza.html?qt=&sc=&alt=. Accessed 13 June 2014.
4. United States Department of Agriculture. Animal and Plant Health Inspection Service, Veterinary Services [USDA APHIS, VS]. Highly pathogenic avian influenza. A threat to U.S. poultry [online]. USDA APHIS, VS; 2002 Feb. Available at: http://www.aphis.usda.gov/oa/pubs/avianflu.html.* Accessed 30 Aug 2004.
5. Brown IH (OIE/FAO/EU International Reference Laboratory for Avian Influenza). Influenza virus infections of pigs. Part 1: swine, avian & human influenza viruses [online]. Available at: http://www.pighealth.com/influenza.htm. Accessed 31 Dec 2006.
6. Olsen CW, Brammer L, Easterday BC, Arden N, Belay E, Baker I, Cox NJ. Serologic evidence of H1 swine Influenza virus infection in swine farm residents and employees. Emerg Infect Dis. 2002;8(8):814-9.
7. Fouchier RA, Munster VJ. Epidemiology of low pathogenic avian influenza viruses in wild birds. Rev Sci Tech. 2009;28(1):49-58.
8. Marchenko VY, Alekseev AY, Sharshov KA, Petrov VN, Silko NY, Susloparov IM, Tserennorov D, Otgonbaatar D, Savchenko IA, Shestopalov AM. Ecology of influenza virus in wild bird populations in Central Asia. Avian Dis. 2012;56(1):234-7.
9. Brown IH. Summary of avian influenza activity in Europe, Asia, and Africa, 2006-2009. Avian Dis. 2010;54(1 Suppl):187-93.
10. Swayne DE. Understanding the complex pathobiology of high pathogenicity avian influenza viruses in birds. Avian Dis. 2007;51(1 Suppl):242-9.
11. World Organization for Animal Health (OIE). Terrestrial animal health code [online]. Paris: OIE; 2014. Avian influenza. Available at: http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_avian_influenza_viruses.htm. Accessed 4 Oct 2014.
12. Centers for Disease Control and Prevention [CDC]. Avian flu [Website online]. CDC; 2014 Jan. Available at: http://www.cdc.gov/flu/avianflu/. Accessed 13 June 2014.
13. World Health Organization [WHO]. Influenza at the human-animal interface. Summary and assessment as of 27 June 2014. WHO; 2014. Available at: http://www.who.int/entity/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_27june14.pdf. Accessed 25 Sept. 2014.
14. World Health Organization (WHO). Confirmed human cases of avian influenza A(H7N9) reported to WHO. Report 17 - data in WHO/HQ as of 08 April 2014. WHO; 2014. Available at http://www.who.int/influenza/human_animal_interface/influenza_h7n9/17_ReportWebH7N9Number_20140408.pdf. Accessed 10 Jun 2014.
15. World Health Organization [WHO]. WHO risk assessment. Human infections with avian influenza A(H7N9) virus 27 June 2014. WHO; 2014 Jun. Available at: http://www.who.int/entity/influenza/human_animal_interface/influenza_h7n9/riskassessment_h7n9_27june14.pdf. Accessed 25 Sept 2014.
16. World Health Organization [WHO]. Influenza at the human-animal interface. Summary and assessment as of 4 September 2015. 2015. WHO; 2015 Sept. Available at: www.who.int/entity/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_04_September_2015.pdf. Accessed 15 Nov 2015.
17. Choi YK, Nguyen TD, Ozaki H, Webby RJ, Puthavathana P, Buranathal C, Chaisingh A, Auewarakul P, Hanh NT, Ma SK, Hui PY, Guan Y, Peiris JS, Webster RG. Studies of H5N1 influenza virus infection of pigs by using viruses isolated in Vietnam and Thailand in 2004. J Virol. 2005;79(16):10821-5.
18. Butler D. Thai dogs carry bird-flu virus, but will they spread it? Nature. 2006;439(7078):773.
19. Takano R, Nidom CA, Kiso M, Muramoto Y, Yamada S, Shinya K, Sakai-Tagawa Y, Kawaoka Y. A comparison of the pathogenicity of avian and swine H5N1 influenza viruses in Indonesia. Arch Virol. 2009;154(4):677-81.
20. Abdel-Moneim AS, Abdel-Ghany AE, Shany SA. Isolation and characterization of highly pathogenic avian influenza virus subtype H5N1 from donkeys. J Biomed Sci. 2010;17:25.
21. Amonsin A, Songserm T, Chutinimitkul S, Jam-On R, Sae-Heng N, Pariyothorn N, Payungporn S, Theamboonlers A, Poovorawan Y. Genetic analysis of influenza A virus (H5N1) derived from domestic cat and dog in Thailand. Arch Virol. 2007;152(10):1925-33.
22. Enserink M, Kaiser J. Virology. Avian flu finds new mammal hosts. Science. 2004;305(5689):1385.
23. Keawcharoen J, Oraveerakul K, Kuiken T, Fouchier RA, Amonsin A, Payungporn S et al. Avian influenza H5N1 in tigers and leopards. Emerg Infect Dis. 2004;10(12):2189-91.
24. Klopfleisch R, Wolf PU, Uhl W, Gerst S, Harder T, Starick E, Vahlenkamp TW, Mettenleiter TC, Teifke JP. 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(3):261-8.
25. Songserm T, Amonsin A, Jam-On R, Sae-Heng N, Meemak N, Pariyothorn N, Payungporn S, Theamboonlers A, Poovorawan Y. Avian influenza H5N1 in naturally infected domestic cat. Emerg Infect Dis. 2006;12(4):681-3.
26. Thanawongnuwech R, Amonsin A, Tantilertcharoen R, Damrongwatanapokin S, Theamboonlers A, Payungporn S et al. Probable tiger-to-tiger transmission of avian influenza H5N1. Emerg Infect Dis. 2005;11(5):699-701.
27. United States Geological Survey [USGS]. National Wildlife Health Center. List of species affected by H5N1 (avian influenza) [online]. USGS; 2013 May. Available at: http://www.nwhc.usgs.gov/disease_information/avian_influenza/affected_species_chart.jsp. Accessed 16 June 2014.
28. World Health Organization (WHO). Avian influenza – H5N1 infection found in a stone marten in Germany [online]. WHO; 2006 March. Available at: http://www.who.int/csr/don/2006_03_09a/en/index.html. Accessed 8 Jan 2006.
29. Yingst SL, Saad MD, Felt SA. Qinghai-like H5N1 from domestic cats, northern Iraq. Emerg Infect Dis. 2006;12(8):1295-7.

30. Songserm T, Amonsin A, Jam-On R, Sae-Heng N, Pariyothorn N, Payungporn S, Theamboonlers A, Chutinimitkul S, Thanawongnuwech R, Poovorawan Y. Fatal avian influenza A H5N1 in a dog. Emerg Infect Dis. 2006;12(11):1744-7.
31. Reperant LA, Rimmelzwaan GF, Kuiken T. Avian influenza viruses in mammals. Rev Sci Tech. 2009;28(1):137-59.
32. Desvaux S, Marx N, Ong S, Gaidet N, Hunt M, Manuguerra JC, Sorn S, Peiris M, van der Werf S, Reynes JM. Highly pathogenic avian influenza virus (H5N1) outbreak in captive wild birds and cats, Cambodia. Emerg Infect Dis. 2009;15(3):475-8.
33. Qi X, Li X, Rider P, Fan W, Gu H, Xu L, Yang Y, Lu S, Wang H, Liu F. Molecular characterization of highly pathogenic H5N1 avian influenza A viruses isolated from raccoon dogs in China. PLoS One. 2009;4(3):e4682.
34. Chen Y, Zhong G, Wang G, Deng G, Li Y, Shi J, Zhang Z, Guan Y, Jiang Y, Bu Z, Kawaoka Y, Chen H. Dogs are highly susceptible to H5N1 avian influenza virus. Virology. 2010;405(1):15-9.
35. Su S, Zhou P, Fu X, Wang L, Hong M, Lu G et al. Virological and epidemiological evidence of avian influenza virus infections among feral dogs in live poultry markets, China: A threat to human health? Clin Infect Dis. 2014;58(11):1644-6.
36. El-Sayed A, Awad W, Fayed A, Hamann HP, Zschock M. Avian influenza prevalence in pigs, Egypt. Emerg Infect Dis. 2010;16(4):726-7.
37. 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(1):54-61.
38. Lin HT, Wang CH, Chueh LL, Su BL, Wang LC. Influenza A(H6N1) Virus in Dogs, Taiwan. Emerg Infect Dis. 2015;21(12):2154-7.
39. Li X, Fu Y, Yang J, Guo J, He J, Guo J, Weng S, Jia Y, Liu B, Li X, Zhu Q, Chen H. Genetic and biological characterization of two novel reassortant H5N6 swine influenza viruses in mice and chickens. Infect Genet Evol. 2015 [Epub ahead of print].
40. Song QQ, Zhang FX, Liu JJ, Ling ZS, Zhu YL, Jiang SJ, Xie ZJ. Dog to dog transmission of a novel influenza virus (H5N2) isolated from a canine. Vet Microbiol. 2013;161(3-4):331-3.
41. Hai-Xia F, Yuan-Yuan L, Qian-Qian S, Zong-Shuai L, Feng-Xia Z, Yan-Li Z, Shi-Jin J, Zhi-Jing X. Interspecies transmission of canine influenza virus H5N2 to cats and chickens by close contact with experimentally infected dogs. Vet Microbiol. 2014;170(3-4):414-7.
42. Zhan GJ, Ling ZS, Zhu YL, Jiang SJ, Xie ZJ. Genetic characterization of a novel influenza A virus H5N2 isolated from a dog in China. Vet Microbiol. 2012;155(2-4):409-16.
43. Sun X, Xu X, Liu Q, Liang D, Li C, He Q, Jiang J, Cui Y, Li J, Zheng L, Guo J, Xiong Y, Yan J. Evidence of avian-like H9N2 influenza A virus among dogs in Guangxi, China. Infect Genet Evol. 2013;20:471-5.
44. Taubenberger JK, Reid AH, Lourens RM, Wang R, Jin G, Fanning TG. Characterization of the 1918 influenza virus polymerase genes. Nature. 2005;437(7060):889-93.
45. Reid AH, Taubenberger JK. The origin of the 1918 pandemic influenza virus: a continuing enigma. J Gen Virol. 2003;84(Pt 9):2285-92.
46. Heinen P. Swine influenza: a zoonosis. Vet Sci Tomorrow [serial online]. 2003 Sept 15. Available at: http://www.vetscite.org/publish/articles/000041/print.html.* Accessed 26 Aug 2004.
47. Taubenberger JK, Kash JC. Influenza virus evolution, host adaptation, and pandemic formation. Cell Host Microbe. 2010;7(6):440-51.
48. Smith GJ, Vijaykrishna D, Bahl J, Lycett SJ, Worobey M, Pybus OG, Ma SK, Cheung CL, Raghwani J, Bhatt S, Peiris JS, Guan Y, Rambaut A. Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic. Nature. 2009;459(7250):1122-5.
49. Vana G, Westover KM. Origin of the 1918 Spanish influenza virus: a comparative genomic analysis. Mol Phylogenet Evol. 2008;47(3):1100-10.
50. Song D, Kang B, Lee C, Jung K, Ha G, Kang D, Park S, Park B, Oh J. Transmission of avian influenza virus (H3N2) to dogs. Emerg Infect Dis. 2008;14(5):741-6.
51. Song D, Lee C, Kang B, Jung K, Oh T, Kim H, Park B, Oh J. Experimental infection of dogs with avian-origin canine influenza A virus (H3N2). Emerg Infect Dis. 2009;15(1):56-8.
52. Zhang YB, Chen JD, Xie JX, Zhu WJ, Wei CY, Tan LK, Cao N, Chen Y, Zhang MZ, Zhang GH, Li SJ. Serologic reports of H3N2 canine influenza virus infection in dogs in Northeast China. J Vet Med Sci. 2013.
53. Li S, Shi Z, Jiao P, Zhang G, Zhong Z, Tian W, Long LP, Cai Z, Zhu X, Liao M, Wan XF. Avian-origin H3N2 canine influenza A viruses in southern China. Infect Genet Evol. 2010;10(8):1286-8.
54. Bunpapong N, Nonthabenjawan N, Chaiwong S, Tangwangvivat R, Boonyapisitsopa S, Jairak W, Tuanudom R, Prakairungnamthip D, Suradhat S, Thanawongnuwech R, Amonsin A. Genetic characterization of canine influenza A virus (H3N2) in Thailand. Virus Genes. 2014;48(1):56-63.
55. Brown IH. History and epidemiology of swine influenza in Europe. Curr Top Microbiol Immunol. 2013;370:133-46.
56. Karasin AI, Schutten MM, Cooper LA, Smith CB, Subbarao K, Anderson GA, Carman S, Olsen CW. Genetic characterization of H3N2 influenza viruses isolated from pigs in North America, 1977-1999: evidence for wholly human and reassortant virus genotypes. Virus Res. 2000;68(1):71-85.
57. Vincent AL, Ma W, Lager KM, Janke BH, Richt JA. Swine influenza viruses a North American perspective. Adv Virus Res. 2008;72:127-54.
58. World Organization for Animal Health [OIE]. Manual of diagnostic tests and vaccines for terrestrial animals [online]. Paris; OIE; 2015. Avian influenza. Available at: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.03.04_AI.pdf. Accessed 1 Jul 2015.
59. Tong S, Li Y, Rivailler P, Conrardy C, Castillo DA, Chen LM et al. A distinct lineage of influenza A virus from bats. Proc Natl Acad Sci U S A. 2012;109(11):4269-74.
60. Tong S, Zhu X, Li Y, Shi M, Zhang J, Bourgeois M et al. New world bats harbor diverse influenza A viruses. PLoS Pathog. 2013;9(10):e1003657.
61. Soda K, Asakura S, Okamatsu M, Sakoda Y, Kida H. H9N2 influenza virus acquires intravenous pathogenicity on the introduction of a pair of di-basic amino acid residues at the cleavage site of the hemagglutinin and consecutive passages in chickens. Virol J. 2011;8:64.

62. Wood GW, Banks J, Strong I, Parsons G, Alexander DJ. An avian influenza virus of H10 subtype that is highly pathogenic for chickens, but lacks multiple basic amino acids at the haemagglutinin cleavage site. Avian Pathol. 1996;25(4):799-806.
63. Gohrbandt S, Veits J, Breithaupt A, Hundt J, Teifke JP, Stech O, Mettenleiter TC, Stech J. H9 avian influenza reassortant with engineered polybasic cleavage site displays a highly pathogenic phenotype in chicken. J Gen Virol. 2011;92(Pt 8):1843-53.
64. Bonfante F, Fusaro A, Zanardello C, Patrono LV, De NR, Maniero S, Terregino C. Lethal nephrotropism of an H10N1 avian influenza virus stands out as an atypical pathotype. Vet Microbiol. 2014;173(3-4):189-200.
65. Veits J, Weber S, Stech O, Breithaupt A, Graber M, Gohrbandt S, Bogs J, Hundt J, Teifke JP, Mettenleiter TC, Stech J. Avian influenza virus hemagglutinins H2, H4, H8, and H14 support a highly pathogenic phenotype. Proc Natl Acad Sci U S A. 2012;109(7):2579-84.
66. Wong SS, Yoon SW, Zanin M, Song MS, Oshansky C, Zaraket H, Sonnberg S, Rubrum A, Seiler P, Ferguson A, Krauss S, Cardona C, Webby RJ, Crossley B. Characterization of an H4N2 influenza virus from quails with a multibasic motif in the hemagglutinin cleavage site. Virology. 2014;468-470C:72-80.
67. Lee CW, Swayne DE, Linares JA, Senne DA, Suarez DL. H5N2 avian influenza outbreak in Texas in 2004: the first highly pathogenic strain in the United States in 20 years? J Virol. 2005;79(17):11412-21.
68. Pelzel AM, McCluskey BJ, Scott AE. Review of the highly pathogenic avian influenza outbreak in Texas, 2004. J Am Vet Med Assoc. 2006;228(12):1869-75.
69. Grebe KM, Yewdell JW, Bennink JR. Heterosubtypic immunity to influenza A virus: where do we stand? Microbes Infect. 2008;10(9):1024-9.
70. Swayne DE. Principles for vaccine protection in chickens and domestic waterfowl against avian influenza: emphasis on Asian H5N1 high pathogenicity avian influenza. Ann N Y Acad Sci. 2006;1081:174-81.
71. Swayne DE, Suarez DL. Current developments in avian influenza vaccines, including safety of vaccinated birds as food. Dev Biol (Basel). 2007;130:123-33.
72. Marangon S, Cecchinato M, Capua I. Use of vaccination in avian influenza control and eradication. Zoonoses Public Health. 2008;55(1):65-72.
73. Kapczynski DR, Swayne DE. Influenza vaccines for avian species. Curr Top Microbiol Immunol. 2009;333:133-52.
74. Lee CW, Saif YM. Avian influenza virus. Comp Immunol Microbiol Infect Dis. 2009;32(4):301-10.
75. Sylte MJ, Suarez DL. Influenza neuraminidase as a vaccine antigen. Curr Top Microbiol Immunol. 2009;333:227-41.
76. Samji T. Influenza A: understanding the viral life cycle. Yale J Biol Med. 2009;82(4):153-9.
77. Ma W, Richt JA. Swine influenza vaccines: current status and future perspectives. Anim Health Res Rev. 2010;11(1):81-96.
78. Couch RB. Orthomyxoviruses [monograph online]. In: Baron S, editor. Medical microbiology. 4th ed. New York: Churchill Livingstone; 1996. Available at: http://www.gsbs.utmb.edu/ microbook/.* Accessed 29 Dec 2006.
79. Fenner F, Bachmann PA, Gibbs EPJ, Murphy FA, Studdert MJ, White DO. Veterinary virology. San Diego, CA: Academic Press Inc.; 1987. Orthomyxoviridae; p. 473-84.
80. Ramey AM, Pearce JM, Ely CR, Guy LM, Irons DB, Derksen DV, Ip HS. Transmission and reassortment of avian influenza viruses at the Asian-North American interface. Virology. 2010;406(2):352-9.
81. Pearce JM, Ramey AM, Ip HS, Gill RE, Jr. Limited evidence of trans-hemispheric movement of avian influenza viruses among contemporary North American shorebird isolates. Virus Res. 2010;148(1-2):44-50.
82. Reeves AB, Pearce JM, Ramey AM, Ely CR, Schmutz JA, Flint PL, Derksen DV, Ip HS, Trust KA. Genomic analysis of avian influenza viruses from waterfowl in western Alaska, USA. J Wildl Dis. 2013;49(3):600-10.
83. Ramey AM, Pearce JM, Flint PL, Ip HS, Derksen DV, Franson JC, Petrula MJ, Scotton BD, Sowl KM, Wege ML, Trust KA. Intercontinental reassortment and genomic variation of low pathogenic avian influenza viruses isolated from northern pintails (Anas acuta) in Alaska: examining the evidence through space and time. Virology. 2010;401(2):179-89.
84. Krauss S, Webster RG. Avian influenza virus surveillance and wild birds: past and present. Avian Dis. 2010;54(1 Suppl):394-8.
85. Wille M, Robertson GJ, Whitney H, Bishop MA, Runstadler JA, Lang AS. Extensive geographic mosaicism in avian influenza viruses from gulls in the northern hemisphere. PLoS One. 2011;6(6):e20664.
86. Hall JS, TeSlaa JL, Nashold SW, Halpin RA, Stockwell T, Wentworth DE, Dugan V, Ip HS. Evolution of a reassortant North American gull influenza virus lineage: drift, shift and stability. Virol J. 2013;10:179.
87. Dusek RJ, Hallgrimsson GT, Ip HS, Jonsson JE, Sreevatsan S, Nashold SW et al. North Atlantic migratory bird flyways provide routes for intercontinental movement of avian influenza viruses. PLoS One. 2014;9(3):e92075.
88. Pearce JM, Ramey AM, Flint PL, Koehler AV, Fleskes JP, Franson JC, Hall JS, Derksen DV, Ip HS. Avian influenza at both ends of a migratory flyway: characterizing viral genomic diversity to optimize surveillance plans for North America. Evol Appl. 2009;2:457-68.
89. Tonnessen R, Kristoffersen AB, Jonassen CM, Hjortaas MJ, Hansen EF, Rimstad E, Hauge AG. Molecular and epidemiological characterization of avian influenza viruses from gulls and dabbling ducks in Norway. Virol J. 2013;10:112.
90. Huang Y, Wille M, Dobbin A, Walzthoni NM, Robertson GJ, Ojkic D, Whitney H, Lang AS. Genetic structure of avian influenza viruses from ducks of the Atlantic flyway of North America. PLoS One. 2014;9(1):e86999.
91. Ramey AM, Reeves AB, Sonsthagen SA, TeSlaa JL, Nashold S, Donnelly T, Casler B, Hall JS. Dispersal of H9N2 influenza A viruses between East Asia and North America by wild birds. Virology. 2015;482:79-83.
92. Hall JS, Hallgrimsson GT, Suwannanarn K, Sreevatsen S, Ip HS, Magnusdottir E, TeSlaa JL, Nashold SW, Dusek RJ. Avian influenza virus ecology in Iceland shorebirds: intercontinental reassortment and movement. Infect Genet Evol. 2014;28:130-6.

93. Gonzalez-Reiche AS, Perez DR. Where do avian influenza viruses meet in the Americas? Avian Dis. 2012;56(4 Suppl):1025-33.

94. Mathieu C, Moreno V, Pedersen J, Jeria J, Agredo M, Gutierrez C, Garcia A, Vasquez M, Avalos P, Retamal P. Avian influenza in wild birds from Chile, 2007-2009. Virus Res. 2015;199:42-5.

95. Bulach D, Halpin R, Spiro D, Pomeroy L, Janies D, Boyle DB. Molecular analysis of H7 avian influenza viruses from Australia and New Zealand: genetic diversity and relationships from 1976 to 2007. J Virol. 2010;84(19):9957-66.

96. Curran JM, Ellis TM, Robertson ID. Surveillance of Charadriiformes in northern Australia shows species variations in exposure to avian influenza virus and suggests negligible virus prevalence. Avian Dis. 2014;58(2):199-204.

97. Hoque MA, Burgess GW, Cheam AL, Skerratt LF. Epidemiology of avian influenza in wild aquatic birds in a biosecurity hotspot, North Queensland, Australia. Prev Vet Med. 2015;118(1):169-81.

98. Yassine HM, Lee CW, Saif YM. Interspecies transmission of influenza A viruses between swine and poultry. Curr Top Microbiol Immunol. 2013;370:227-40.

99. Tremblay D, Allard V, Doyon JF, Bellehumeur C, Spearman JG, Harel J, Gagnon CA. Emergence of a new swine H3N2 and pandemic (H1N1) 2009 influenza A virus reassortant in two Canadian animal populations, mink and swine. J Clin Microbiol. 2011;49(12):4386-90.

100. Hinshaw VS, Bean WJ, Webster RG, Rehg JE, Fiorelli P, Early G, Geraci JR, St Aubin DJ. Are seals frequently infected with avian influenza viruses? J Virol. 1984;51(3):863-5.

101. Crawford PC, Dubovi EJ, Castleman WL, Stephenson I, Gibbs EP, Chen L et al. Transmission of equine influenza virus to dogs. Science. 2005;310(5747):482-5.

102. Daly JM, Blunden AS, Macrae S, Miller J, Bowman SJ, Kolodziejek J, Nowotny N, Smith KC. Transmission of equine influenza virus to English foxhounds. Emerg Infect Dis. 2008;14(3):461-4.

103. Gagnon CA, Spearman G, Hamel A, Godson DL, Fortin A, Fontaine G, Tremblay D. Characterization of a Canadian mink H3N2 influenza A virus isolate genetically related to triple reassortant swine influenza virus. J Clin Microbiol. 2009;47(3):796-9.

104. Patterson AR, Cooper VL, Yoon KJ, Janke BH, Gauger PC. Naturally occurring influenza infection in a ferret (*Mustela putorius furo*) colony. J Vet Diagn Invest. 2009;21(4):527-30.

105. Enserink M. Epidemiology. Horse flu virus jumps to dogs. Science. 2005;309(5744):2147.

106. Payungporn S, Crawford PC, Kouo TS, Chen LM, Pompey J, Castleman WL, Dubovi EJ, Katz JM, Donis RO. Influenza A virus (H3N8) in dogs with respiratory disease, Florida. Emerg Infect Dis. 2008;14(6):902-8.

107. Chen H, Deng G, Li Z, Tian G, Li Y, Jiao P, Zhang L, Liu Z, Webster RG, Yu K. The evolution of H5N1 influenza viruses in ducks in southern China. Proc Natl Acad Sci U S A. 2004;101(28):10452-7.

108. Krauss S, Stallknecht DE, Negovetich NJ, Niles LJ, Webby RJ, Webster RG. Coincident ruddy turnstone migration and horseshoe crab spawning creates an ecological 'hot spot' for influenza viruses. Proc Biol Sci. 2010;277(1699):3373-9.

109. Tolf C, Bengtsson D, Rodrigues D, Latorre-Margalef N, Wille M, Figueiredo ME, Jankowska-Hjortaas M, Germundsson A, Duby PY, Lebarbenchon C, Gauthier-Clerc M, Olsen B, Waldenstrom J. Birds and viruses at a crossroad--surveillance of influenza A virus in Portuguese waterfowl. PLoS One. 2012;7(11):e49002.

110. Parmley J, Lair S, Leighton FA. Canada's inter-agency wild bird influenza survey. Integr Zool. 2009;4(4):409-17.

111. Germundsson A, Madslien KI, Hjortaas MJ, Handeland K, Jonassen CM. Prevalence and subtypes of influenza A viruses in wild waterfowl in Norway 2006-2007. Acta Vet Scand. 2010;52:28.

112. Ely CR, Hall JS, Schmutz JA, Pearce JM, Terenzi J, Sedinger JS, Ip HS. Evidence that life history characteristics of wild birds influence infection and exposure to influenza A viruses. PLoS One. 2013;8(3):e57614.

113. Lebarbenchon C, Sreevatsan S, Ramakrishnan MA, Poulson R, Goekjian V, Di Matteo JJ, Wilcox B, Stallknecht DE. Influenza A viruses in American White Pelican (*Pelecanus erythrorhynchos*). J Wildl Dis. 2010;46(4):1284-9.

114. Siembieda JL, Johnson CK, Cardona C, Anchell N, Dao N, Reisen W, Boyce W. Influenza A viruses in wild birds of the Pacific flyway, 2005-2008. Vector Borne Zoonotic Dis. 2010;10(8):793-800.

115. Roslaia IG, Roslaiakov GE, Lvov DK. [Isolation of influenza A viruses and detection of antibodies in common herons (*Ardea cinera*) nesting in the lower Amur]. Ekol Virusov. 1975;3:138-42.

116. Wille M, Huang Y, Robertson GJ, Ryan P, Wilhelm SI, Fifield D et al. Evaluation of seabirds in Newfoundland and Labrador, Canada, as hosts of influenza A viruses. J Wildl Dis. 2014;50(1):98-103.

117. Piaggio AJ, Shriner SA, VanDalen KK, Franklin AB, Anderson TD, Kolokotronis SO. Molecular surveillance of low pathogenic avian influenza viruses in wild birds across the United States: inferences from the hemagglutinin gene. PLoS One. 2012;7(12):e50834.

118. Kang HM, Jeong OM, Kim MC, Kwon JS, Paek MR, Choi JG, Lee EK, Kim YJ, Kwon JH, Lee YJ. Surveillance of avian influenza virus in wild bird fecal samples from South Korea, 2003-2008. J Wildl Dis. 2010;46(3):878-88.

119. Brown J, Poulson R, Carter D, Lebarbenchon C, Pantin-Jackwood M, Spackman E, Shepherd E, Killian M, Stallknecht D. Susceptibility of avian species to North American H13 low pathogenic avian influenza viruses. Avian Dis. 2012;56(4 Suppl):969-75.

120. Verhagen JH, Majoor F, Lexmond P, Vuong O, Kasemir G, Lutterop D, Osterhaus AD, Fouchier RA, Kuiken T. Epidemiology of influenza A virus among black-headed gulls, the Netherlands, 2006-2010. Emerg Infect Dis. 2014;20(1):138-41.

121. Kawaoka Y, Yamnikova S, Chambers TM, Lvov DK, Webster RG. Molecular characterization of a new hemagglutinin, subtype H14, of influenza A virus. Virology. 1990;179(2):759-67.

122. Nolting J, Fries AC, Slemons RD, Courtney C, Hines N, Pedersen J. Recovery of H14 influenza A virus isolates from sea ducks in the Western Hemisphere. PLoS Curr. 2012;4:RRN1290.

123. Fries AC, Nolting JM, Bowman AS, Killian ML, Wentworth DE, Slemons RD. Genomic analyses detect Eurasian-lineage H10 and additional H14 influenza A viruses recovered from waterfowl in the Central United States. Influenza Other Respir Viruses. 20148(4):493-8.

124. Boyce WM, Schobel S, Dugan VG, Halpin R, Lin X, Wentworth DE, Lindsay LL, Mertens E, Plancarte M. Complete genome sequence of a reassortant H14N2 avian influenza virus from California. Genome Announc. 2013;1(4).

125. Fereidouni SR, Harder TC, Globig A, Starick E. Failure of productive infection of mallards (*Anas platyrhynchos*) with H16 subtype of avian influenza viruses. Influenza Other Respir Viruses. 2014;8(6):613-6.

126. Hesterberg U, Harris K, Stroud D, Guberti V, Busani L, Pittman M, Piazza V, Cook A, Brown I. Avian influenza surveillance in wild birds in the European Union in 2006. Influenza Other Respi Viruses. 2009;3(1):1-14.

127. Brown JD, Luttrell MP, Berghaus RD, Kistler W, Keeler SP, Howey A, Wilcox B, Hall J, Niles L, Dey A, Knutsen G, Fritz K, Stallknecht DE. Prevalence of antibodies to type a influenza virus in wild avian species using two serologic assays. J Wildl Dis. 2010;46(3):896-911.

128. Thinh TV, Gilbert M, Bunpapong N, Amonsin A, Nguyen DT, Doherty PF, Jr., Huyvaert KP. Avian influenza viruses in wild land birds in northern Vietnam. J Wildl Dis. 2012;48(1):195-200.

129. Olsen B, Munster VJ, Wallensten A, Waldenstrom J, Osterhaus AD, Fouchier RA. Global patterns of influenza a virus in wild birds. Science. 2006;312(5772):384-8.

130. Stallknecht DE, Brown JD. Wild birds and the epidemiology of avian influenza. J Wildl Dis. 2007;43 Suppl:S15-20.

131. Abolnik C. A current review of avian influenza in pigeons and doves (Columbidae). Vet Microbiol. 2014;170(3-4):181-96.

132. Nemeth NM, Oesterle PT, Poulson RL, Jones CA, Tompkins SM, Brown JD, Stallknecht DE. Experimental infection of European starlings (*Sturnus vulgaris*) and house sparrows (*Passer domesticus*) with pandemic 2009 H1N1 and swine H1N1 and H3N2 triple reassortant influenza vFiebig2011iruses. J Wildl Dis. 2013;49(2):437-40.

133. Goyal SM, Jindal N, Chander Y, Ramakrishnan MA, Redig PT, Sreevatsan S. Isolation of mixed subtypes of influenza A virus from a bald eagle (*Haliaeetus leucocephalus*). Virol J. 2010;7:174.

134. Fuller TL, Saatchi SS, Curd EE, Toffelmier E, Thomassen HA, Buermann W, DeSante DF, Nott MP, Saracco JF, Ralph C, Alexander JD, Pollinger JP, Smith TB. Mapping the risk of avian influenza in wild birds in the US. BMC Infect Dis. 2010;10:187.

135. Slusher MJ, Wilcox BR, Lutrell MP, Poulson RL, Brown JD, Yabsley MJ, Stallknecht DE. Are passerine birds reservoirs for influenza A viruses? J Wildl Dis. 2014;50(4):792-809.

136. Fuller TL, Ducatez MF, Njabo KY, Couacy-Hymann E, Chasar A, Aplogan GL, Lao S, Awoume F, Tehou A, Langeois Q, Krauss S, Smith TB. Avian influenza surveillance in Central and West Africa, 2010-2014. Epidemiol Infect. 2015;143(10):2205-12.

137. Kim HR, Kwon YK, Jang I, Lee YJ, Kang HM, Lee EK, Song BM, Lee HS, Joo YS, Lee KH, Lee HK, Baek KH, Bae YC. Pathologic changes in wild birds infected with highly pathogenic avian influenza A(H5N8) viruses, South Korea, 2014. Emerg Infect Dis. 2015;21(5):775-80.

138. Verhagen JH, van der Jeugd HP, Nolet BA, Slaterus R, Kharitonov SP, de Vries PP, Vuong O, Majoor F, Kuiken T, Fouchier RA. Wild bird surveillance around outbreaks of highly pathogenic avian influenza A(H5N8) virus in the Netherlands, 2014, within the context of global flyways. Euro Surveill. 2015;20(12).. pii: 21069.

139. Becker WB. The isolation and classification of Tern virus: influenza A-Tern South Africa--1961. J Hyg (Lond). 1966;64(3):309-20.

140. Gaidet N, Cattoli G, Hammoumi S, Newman SH, Hagemeijer W, Takekawa JY et al. Evidence of infection by H5N2 highly pathogenic avian influenza viruses in healthy wild waterfowl. PLoS Pathog. 2008;4(8):e1000127.

141. Kaleta EF, Honicke A. A retrospective description of a highly pathogenic avian influenza A virus (H7N1/Carduelis/Germany/72) in a free-living siskin (C*arduelis spinus* Linnaeus, 1758) and its accidental transmission to yellow canaries (*Serinus canaria* Linnaeus, 1758). Dtsch Tierarztl Wochenschr. 2005;112(1):17-9.

142. Gilbert M, Xiao X, Domenech J, Lubroth J, Martin V, Slingenbergh J. Anatidae migration in the western Palearctic and spread of highly pathogenic avian influenza H5NI virus. Emerg Infect Dis. 2006;12(11):1650-6.

143. Nagy A, Machova J, Hornickova J, Tomci M, Nagl I, Horyna B, Holko I. Highly pathogenic avian influenza virus subtype H5N1 in mute swans in the Czech Republic. Vet Microbiol. 2007;120(1-2):9-16.

144. Teifke JP, Klopfleisch R, Globig A, Starick E, Hoffmann B, Wolf PU, Beer M, Mettenleiter TC, Harder TC. Pathology of natural infections by H5N1 highly pathogenic avian influenza virus in mute (*Cygnus olor*) and whooper (*Cygnus cygnus*) swans. Vet Pathol. 2007;44(2):137-43.

145. Ellis TM, Leung CY, Chow MK, Bissett LA, Wong W, Guan Y, Malik Peiris JS. Vaccination of chickens against H5N1 avian influenza in the face of an outbreak interrupts virus transmission. Avian Pathol. 2004;33(4):405-12.

146. Liu J, Xiao H, Lei F, Zhu Q, Qin K, Zhang XW, Zhang XL, Zhao D, Wang G, Feng Y, Ma J, Liu W, Wang J, Gao GF. Highly pathogenic H5N1 influenza virus infection in migratory birds. Science. 2005;309(5738):1206.

147. Lei F, Tang S, Zhao D, Zhang X, Kou Z, Li Y, Zhang Z, Yin Z, Chen S, Li S, Zhang D, Yan B, Li T. Characterization of H5N1 influenza viruses isolated from migratory birds in Qinghai province of China in 2006. Avian Dis. 2007;51(2):568-72.

148. Brown JD, Stallknecht DE, Beck JR, Suarez DL, Swayne DE. Susceptibility of North American ducks and gulls to H5N1 highly pathogenic avian influenza viruses. Emerg Infect Dis. 2006;12(11):1663-70.

149. Sturm-Ramirez KM, Ellis T, Bousfield B, Bissett L, Dyrting K, Rehg JE, Poon L, Guan Y, Peiris M, Webster RG. Reemerging H5N1 influenza viruses in Hong Kong in 2002 are highly pathogenic to ducks. J Virol. 2004;78(9):4892-901.

150. Isoda N, Sakoda Y, Kishida N, Bai GR, Matsuda K, Umemura T, Kida H. Pathogenicity of a highly pathogenic avian influenza virus, A/chicken/Yamaguchi/7/04 (H5N1) in different species of birds and mammals. Arch Virol. 2006;151(7):1267-79.
151. Perkins LE, Swayne DE. Varied pathogenicity of a Hong Kong-origin H5N1 avian influenza virus in four passerine species and budgerigars. Vet Pathol. 2003;40(1):14-24.
152. Boon AC, Sandbulte MR, Seiler P, Webby RJ, Songserm T, Guan Y, Webster RG. Role of terrestrial wild birds in ecology of influenza A virus (H5N1). Emerg Infect Dis. 2007;13(11):1720-4.
153. Khan SU, Berman L, Haider N, Gerloff N, Rahman MZ, Shu B et al. Investigating a crow die-off in January-February 2011 during the introduction of a new clade of highly pathogenic avian influenza virus H5N1 into Bangladesh. Arch Virol. 2014;159(3):509-18.
154. Siengsanan J, Chaichoune K, Phonaknguen R, Sariya L, Prompiram P, Kocharin W, Tangsudjai S, Suwanpukdee S, Wiriyarat W, Pattanarangsan R, Robertson I, Blacksell SD, Ratanakorn P. Comparison of outbreaks of H5N1 highly pathogenic avian influenza in wild birds and poultry in Thailand. J Wildl Dis. 2009;45(3):740-7.
155. Chang H, Dai F, Liu Z, Yuan F, Zhao S, Xiang X, Zou F, Zeng B, Fan Y, Duan G. Seroprevalence survey of avian influenza A (H5) in wild migratory birds in Yunnan Province, Southwestern China. Virol J. 2014;11:18.
156. U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services [USDA APHIS, VS]. Update on avian influenza findings in the Pacific flyway. Available at: http://www.aphis.usda.gov/wps/portal/?urile=wcm:path:/aphis_content_library/sa_our_focus/sa_animal_health/sa_animal_disease_information/sa_avian_health. Accessed 6 Feb 2015.
157. Shin JH, Woo C, Wang SJ, Jeong J, An IJ, Hwang JK, Jo SD, Yu SD, Choi K, Chung HM, Suh JH, Kim SH. Prevalence of avian influenza virus in wild birds before and after the HPAI H5N8 outbreak in 2014 in South Korea. J Microbiol. 2015;53(7):475-80.
158. Lee DH, Torchetti MK, Winker K, Ip HS, Song CS, Swayne DE. Intercontinental spread of Asian-origin H5N8 to North America through Beringia by migratory birds. J Virol. 2015;89(12):6521-4.
159. Pasick J, Berhane Y, Joseph T, Bowes V, Hisanaga T, Handel K, Alexandersen S. Reassortant highly pathogenic influenza A H5N2 virus containing gene segments related to Eurasian H5N8 in British Columbia, Canada, 2014. Sci Rep. 2015;5:9484.
160. Ip HS, Torchetti MK, Crespo R, Kohrs P, DeBruyn P, Mansfield KG et al. Novel Eurasian highly pathogenic avian influenza A H5 viruses in wild birds, Washington, USA, 2014. Emerg Infect Dis. 2015;21(5):886-90.
161. Bouwstra R, Heutink R, Bossers A, Harders F, Koch G, Elbers A. Full-Genome sequence of influenza A(H5N8) virus in poultry linked to sequences of strains from Asia, the Netherlands, 2014. Emerg Infect Dis. 2015;21(5):872-4.
162. Hill SC, Lee YJ, Song BM, Kang HM, Lee EK, Hanna A, Gilbert M, Brown IH, Pybus OG. Wild waterfowl migration and domestic duck density shape the epidemiology of highly pathogenic H5N8 influenza in the Republic of Korea. Infect Genet Evol. 2015 [Epub ahead of print].
163. Kwon YK, Joh SJ, Kim MC, Sung HW, Lee YJ, Choi JG, Lee EK, Kim JH. Highly pathogenic avian influenza (H5N1) in the commercial domestic ducks of South Korea. Avian Pathol. 2005;34(4):367-70.
164. Alexander DJ, Parsons G, Manvell RJ. Experimental assessment of the pathogenicity of eight avian influenza A viruses of H5 subtype for chickens, turkeys, ducks and quail. Avian Pathol. 1986;15(4):647-62.
165. Perkins LE, Swayne DE. Pathobiology of A/chicken/Hong Kong/220/97 (H5N1) avian influenza virus in seven gallinaceous species. Vet Pathol. 2001;38(2):149-64.
166. Wood JM, Webster RG, Nettles VF. Host range of A/Chicken/Pennsylvania/83 (H5N2) influenza virus. Avian Dis. 1985;29(1):198-207.
167. van der Goot JA, van BM, Koch G, de Jong MC. Variable effect of vaccination against highly pathogenic avian influenza (H7N7) virus on disease and transmission in pheasants and teals. Vaccine. 2007;25(49):8318-25.
168. Wood GW, Parsons G, Alexander DJ. Replication of influenza A viruses of high and low pathogenicity for chickens at different sites in chickens and ducks following intranasal inoculation. Avian Pathol. 1995;24(3):545-51.
169. Alexander DJ, Allan WH, Parsons DG, Parsons G. The pathogenicity of four avian influenza viruses for fowls, turkeys and ducks. Res Vet Sci. 1978;24(2):242-7.
170. Westbury HA, Turner AJ, Kovesdy L. The pathogenicity of three Australian fowl plague viruses for chickens, turkeys and ducks. Vet Microbiol. 1979;4:223-34.
171. Sturm-Ramirez KM, Hulse-Post DJ, Govorkova EA, Humberd J, Seiler P, Puthavathana P et al. Are ducks contributing to the endemicity of highly pathogenic H5N1 influenza virus in Asia? J Virol. 2005;79(17):11269-79.
172. Yamamoto Y, Nakamura K, Kitagawa K, Ikenaga N, Yamada M, Mase M, Narita M. Severe nonpurulent encephalitis with mortality and feather lesions in call ducks (Anas platyrhyncha var. domestica) inoculated intravenously with H5N1 highly pathogenic avian influenza virus. Avian Dis. 2007;51(1):52-7.
173. Hulse-Post DJ, Sturm-Ramirez KM, Humberd J, Seiler P, Govorkova EA, Krauss S et al. Role of domestic ducks in the propagation and biological evolution of highly pathogenic H5N1 influenza viruses in Asia. Proc Natl Acad Sci U S A. 2005;102(30):10682-7.
174. Kishida N, Sakoda Y, Isoda N, Matsuda K, Eto M, Sunaga Y, Umemura T, Kida H. Pathogenicity of H5 influenza viruses for ducks. Arch Virol. 2005;150(7):1383-92.
175. Tian G, Zhang S, Li Y, Bu Z, Liu P, Zhou J, Li C, Shi J, Yu K, Chen H. Protective efficacy in chickens, geese and ducks of an H5N1-inactivated vaccine developed by reverse genetics. Virology. 2005;341(1):153-62.
176. Webster RG, Webby RJ, Hoffmann E, Rodenberg J, Kumar M, Chu HJ, Seiler P, Krauss S, Songserm T. The immunogenicity and efficacy against H5N1 challenge of reverse genetics-derived H5N3 influenza vaccine in ducks and chickens. Virology. 2006;351(2):303-11.

177. Beato MS, Toffan A, De Nardi R., Cristalli A, Terregino C, Cattoli G, Capua I. A conventional, inactivated oil emulsion vaccine suppresses shedding and prevents viral meat colonisation in commercial (Pekin) ducks challenged with HPAI H5N1. Vaccine. 2007;25(20):4064-72.

178. Middleton D, Bingham J, Selleck P, Lowther S, Gleeson L, Lehrbach P, Robinson S, Rodenberg J, Kumar M, Andrew M. Efficacy of inactivated vaccines against H5N1 avian influenza infection in ducks. Virology. 2007;359(1):66-71.

179. Alexander DY. A review of avian influenza [monograph online]. Available at: http://www.esvv.unizh.ch/gent_abstracts/Alexander.html.* Accessed 30 Aug 2004.

180. Promed Mail. Avian influenza, ostriches - South Africa. Aug 7, 2004. Archive Number 20040807.2176. Available at http://www.promedmail.org. Accessed 10 Jan 2007.

181. Promed Mail. Avian influenza, ostriches – South Africa (H5N2)(03): OIE. July 18, 2006. Archive Number 20060718.1970. Available at: http://www.promedmail.org. Accessed 10 Jan 2007.

182. Manvell RJ, English C, Jorgensen PH, Brown IH. Pathogenesis of H7 influenza A viruses isolated from ostriches in the homologous host infected experimentally. Avian Dis. 2003;47(3 Suppl):1150-3.

183. Shinde PV, Koratkar SS, Pawar SD, Kale SD, Rawankar AS, Mishra AC. Serologic evidence of avian influenza H9N2 and paramyxovirus type 1 infection in emus (*Dromaius novaehollandiae*) in India. Avian Dis. 2012;56(1):257-60.

184. Toffan A, Olivier A, Mancin M, Tuttoilmondo V, Facco D, Capua I, Terregino C. Evaluation of different serological tests for the detection of antibodies against highly pathogenic avian influenza in experimentally infected ostriches (*Struthio camelus*). Avian Pathol. 2010;39(1):11-5.

185. Olivier AJ. Ecology and epidemiology of avian influenza in ostriches. Dev Biol (Basel). 2006;124:51-7.

186. Capua I, Mutinelli F, Terregino C, Cattoli G, Manvell RJ, Burlini F. Highly pathogenic avian influenza (H7N1) in ostriches farmed in Italy. Vet Rec. 2000;146(12):356.

187. Abolnik C, Olivier AJ, Grewar J, Gers S, Romito M. Molecular analysis of the 2011 HPAI H5N2 outbreak in ostriches, South Africa. Avian Dis. 2012;56(4 Suppl):865-79.

188. Howerth EW, Olivier A, Franca M, Stallknecht DE, Gers S. Pathobiology of highly pathogenic avian influenza virus H5N2 infection in juvenile ostriches from South Africa. Avian Dis. 2012;56(4 Suppl):966-8.

189. Ismail MM, El-Sabagh IM, Al-Ankari AR. Characterization and phylogenetic analysis of a highly pathogenic avian influenza H5N1 virus isolated from diseased ostriches (*Struthio camelus*) in the Kingdom of Saudi Arabia. Avian Dis. 2014;58(2):309-12.

190. Leschnik M, Weikel J, Mostl K, Revilla-Fernandez S, Wodak E, Bago Z, Vanek E, Benetka V, Hess M, Thalhammer JG. Subclinical infection with avian influenza A (H5N1) virus in cats. Emerg Infect Dis. 2007;13(2):243-7.

191. Zhou J, Sun W, Wang J, Guo J, Yin W, Wu N, Li L, Yan Y, Liao M, Huang Y, Luo K, Jiang X, Chen H. Characterization of the H5N1 highly pathogenic avian influenza virus derived from wild pikas in China. J Virol. 2009;83(17):8957-64.

192. Choi YK, Pascua PN, Song MS. Swine influenza viruses: an Asian perspective. Curr Top Microbiol Immunol. 2013;370:147-72.

193. Zhu H, Webby R, Lam TT, Smith DK, Peiris JS, Guan Y. History of swine influenza viruses in Asia. Curr Top Microbiol Immunol. 2013;370:57-68.

194. Cong YL, Pu J, Liu QF, Wang S, Zhang GZ, Zhang XL, Fan WX, Brown EG, Liu JH. Antigenic and genetic characterization of H9N2 swine influenza viruses in China. J Gen Virol. 2007;88(Pt 7):2035-41.

195. Monne I, Cattoli G, Mazzacan E, Amarin NM, Al Maaitah HM, Al-Natour MQ, Capua I. Genetic comparison of H9N2 AI viruses isolated in Jordan in 2003. Avian Dis. 2007;51(1 Suppl):451-4.

196. Wang N, Zou W, Yang Y, Guo X, Hua Y, Zhang Q, Zhao Z, Jin M. Complete genome sequence of an H10N5 avian influenza virus isolated from pigs in central China. J Virol. 2012;86(24):13865-6.

197. Zhang G, Kong W, Qi W, Long LP, Cao Z, Huang L, Qi H, Cao N, Wang W, Zhao F, Ning Z, Liao M, Wan XF. Identification of an H6N6 swine influenza virus in southern China. Infect Genet Evol. 2011;11(5):1174-7.

198. Lee JH, Pascua PN, Song MS, Baek YH, Kim CJ, Choi HW, Sung MH, Webby RJ, Webster RG, Poo H, Choi YK. Isolation and genetic characterization of H5N2 influenza viruses from pigs in Korea. J Virol. 2009;83(9):4205-15.

199. Zhao G, Chen C, Huang J, Wang Y, Peng D, Liu X. Characterisation of one H6N6 influenza virus isolated from swine in China. Res Vet Sci. 2013;95(2):434-6.

200. He L, Zhao G, Zhong L, Liu Q, Duan Z, Gu M, Wang X, Liu X, Liu X. Isolation and characterization of two H5N1 influenza viruses from swine in Jiangsu Province of China. Arch Virol. 2013;158(12):2531-41.

201. Yu Z, Cheng K, Sun W, Xin Y, Cai J, Ma R et al. Lowly pathogenic avian influenza (H9N2) infection in Plateau pika (*Ochotona curzoniae*), Qinghai Lake, China. Vet Microbiol. 2014;173(1-2):132-5.

202. Zohari S, Neimanis A, Harkonen T, Moraeus C, Valarcher JF. Avian influenza A(H10N7) virus involvement in mass mortality of harbour seals (*Phoca vitulina*) in Sweden, March through October 2014. Euro Surveill. 2014;19(46). pii: 20967.

203. Peng L, Chen C, Kai-yi H, Feng-Xia Z, Yan-Li Z, Zong-Shuai L, Xing-xiao Z, Shi-Jin J, Zhi-Jing X. Molecular characterization of H9N2 influenza virus isolated from mink and its pathogenesis in mink. Vet Microbiol. 2015;176(1-2):88-96.

204. World Health Organization [WHO]. Avian influenza ("bird flu") fact sheet [online]. WHO; 2014 Mar. Available at: http://www.who.int/mediacentre/factsheets/avian_influenza/en/#humans. Accessed 13 June 2014.

205. Eagles D, Siregar ES, Dung DH, Weaver J, Wong F, Daniels P. H5N1 highly pathogenic avian influenza in Southeast Asia. Rev Sci Tech. 2009;28(1):341-8.

206. Smith GJ, Fan XH, Wang J, Li KS, Qin K, Zhang JX, Vijaykrishna D, Cheung CL, Huang K, Rayner JM, Peiris JS, Chen H, Webster RG, Guan Y. Emergence and predominance of an H5N1 influenza variant in China. Proc Natl Acad Sci U S A. 2006;103(45):16936-41.

207. Guan Y, Smith GJ, Webby R, Webster RG. Molecular epidemiology of H5N1 avian influenza. Rev Sci Tech. 2009;28(1):39-47.

208. Uyeki TM. Human infection with highly pathogenic avian influenza A (H5N1) virus: review of clinical issues. Clin Infect Dis. 2009;49(2):279-90.

209. Kim JK, Seiler P, Forrest HL, Khalenkov AM, Franks J, Kumar M, Karesh WB, Gilbert M, Sodnomdarjaa R, Douangngeun B, Govorkova EA, Webster RG. Pathogenicity and vaccine efficacy of different clades of Asian H5N1 avian influenza A viruses in domestic ducks. J Virol. 2008;82(22):11374-82.

210. WHO/OIE/FAO H5N1 Evolution Working Group. Continuing progress towards a unified nomenclature for the highly pathogenic H5N1 avian influenza viruses: divergence of clade 2.2 viruses. Influenza Other Respi Viruses. 2009;3(2):59-62.

211. Govorkova EA, Rehg JE, Krauss S, Yen HL, Guan Y, Peiris M, Nguyen TD, Hanh TH, Puthavathana P, Long HT, Buranathai C, Lim W, Webster RG, Hoffmann E. Lethality to ferrets of H5N1 influenza viruses isolated from humans and poultry in 2004. J Virol. 2005;79(4):2191-8.

212. Zhao K, Gu M, Zhong L, Duan Z, Zhang Y, Zhu Y, Zhao G, Zhao M, Chen Z, Hu S, Liu W, Liu X, Peng D, Liu X. Characterization of three H5N5 and one H5N8 highly pathogenic avian influenza viruses in China. Vet Microbiol. 2013;163(3-4):351-7.

213. Gu M, Liu W, Cao Y, Peng D, Wang X, Wan H, Zhao G, Xu Q, Zhang W, Song Q, Li Y, Liu X. Novel reassortant highly pathogenic avian influenza (H5N5) viruses in domestic ducks, China. Emerg Infect Dis. 2011;17(6):1060-3.

214. Zou W, Guo X, Li S, Yang Y, Jin M. Complete genome sequence of a novel natural recombinant H5N5 influenza virus from ducks in central China. J Virol. 2012;86(24):13878.

215. Zhao G, Gu X, Lu X, Pan J, Duan Z, Zhao K et al. Novel reassortant highly pathogenic H5N2 avian influenza viruses in poultry in China. PLoS One. 2012;7(9):e46183.

216. Nishi T, Okamatsu M, Sakurai K, Chu HD, Thanh LP, VAN NL, VAN HN, Thi DN, Sakoda Y, Kida H. Genetic analysis of an H5N2 highly pathogenic avian influenza virus isolated from a chicken in a live bird market in Northern Vietnam in 2012. J Vet Med Sci. 2014;76(1):85-7.

217. Liu CG, Liu M, Liu F, Lv R, Liu DF, Qu LD, Zhang Y. Emerging multiple reassortant H5N5 avian influenza viruses in ducks, China, 2008. Vet Microbiol. 2013;167(3-4):296-306.

218. Bi Y, Mei K, Shi W, Liu D, Yu X, Gao Z, Zhao L, Gao GF, Chen J, Chen Q. Two novel reassortants of avian influenza A (H5N6) virus in China. J Gen Virol. 2015;96(Pt 5):975-81.

219. European Food Safety Authority (EFSA). Highly pathogenic avian influenza A subtype H5N8. EFSA J. 2014;12(12):3941.

220. Jhung MA, Nelson DI. Outbreaks of avian influenza A (H5N2), (H5N8), and (H5N1) among birds--United States, December 2014-January 2015. MMWR Morb Mortal Wkly Rep. 2015;64(4):111.

221. Clement T, Kutish GF, Nezworski J, Scaria J, Nelson E, Christopher-Hennings J, Diel DG. Complete genome sequence of a highly pathogenic avian influenza virus (H5N2) associated with an outbreak in commercial chickens, Iowa, USA, 2015. Genome Announc. 2015;3(3).

222. Torchetti MK, Killian ML, Dusek RJ, Pedersen JC, Hines N, Bodenstein B, White CL, Ip HS. Novel H5 Clade 2.3.4.4 reassortant (H5N1) virus from a green-winged teal in Washington, USA. Genome Announc. 2015;3(2).

223. World Organization for Animal Health [OIE]. Summary of immediate notifications and follow-ups–2015. Highly pathogenic avian influenza. World Animal Health Information Database (WAHID) Interface [database online]. Available at: http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/Immsummary. Accessed 7 Jul 2015.

224. Weber TP, Stilianakis NI. Ecologic immunology of avian influenza (H5N1) in migratory birds. Emerg Infect Dis. 2007;13(8):1139-43.

225. Feare CJ. Role of wild birds in the spread of highly pathogenic avian influenza virus H5N1 and implications for global surveillance. Avian Dis. 2010;54(1 Suppl):201-12.

226. Beato MS, Capua I. Transboundary spread of highly pathogenic avian influenza through poultry commodities and wild birds: a review. Rev Sci Tech. 2011;30(1):51-61.

227. Kwon YK, Thomas C, Swayne DE. Variability in pathobiology of South Korean H5N1 high-pathogenicity avian influenza virus infection for 5 species of migratory waterfowl. Vet Pathol. 2010;47(3):495-506.

228. El-Sayed A, Prince A, Fawzy A, Nadra E, Abdou MI, Omar L, Fayed A, Salem M. Sero-prevalence of avian influenza in animals and human in Egypt. Pak J Biol Sci. 2013;16(11):524-9.

229. Horimoto T, Maeda K, Murakami S, Kiso M, Iwatsuki-Horimoto K, Sashika M, Ito T, Suzuki K, Yokoyama M, Kawaoka Y. Highly pathogenic avian influenza virus infection in feral raccoons, Japan. Emerg Infect Dis. 2011;17(4):714-7.

230. Yamaguchi E, Sashika M, Fujii K, Kobayashi K, Bui VN, Ogawa H, Imai K. Prevalence of multiple subtypes of influenza A virus in Japanese wild raccoons. Virus Res. 2014;189:8-13.

231. Guan Y, Peiris JS, Lipatov AS, Ellis TM, Dyrting KC, Krauss S, Zhang LJ, Webster RG, Shortridge KF. Emergence of multiple genotypes of H5N1 avian influenza viruses in Hong Kong SAR. Proc Natl Acad Sci U S A. 2002;99(13):8950-5.

232. Kuiken T, Rimmelzwaan G, van RD, van AG, Baars M, Fouchier R, Osterhaus A. Avian H5N1 influenza in cats. Science. 2004;306(5694):241.

233. Perkins LE, Swayne DE. Comparative susceptibility of selected avian and mammalian species to a Hong Kong-origin H5N1 high-pathogenicity avian influenza virus. Avian Dis. 2003;47(3 Suppl):956-67.

234. Rimmelzwaan GF, van Riel D., Baars M, Bestebroer TM, van Amerongen G., Fouchier RA, Osterhaus AD, Kuiken T. 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(1):176-83.

235. Lipatov AS, Kwon YK, Sarmento LV, Lager KM, Spackman E, Suarez DL, Swayne DE. Domestic pigs have low susceptibility to H5N1 highly pathogenic avian influenza viruses. PLoS Pathog. 2008;4(7):e1000102.

236. Giese M, Harder TC, Teifke JP, Klopfleisch R, Breithaupt A, Mettenleiter TC, Vahlenkamp TW. Experimental infection and natural contact exposure of dogs with avian influenza virus (H5N1). Emerg Infect Dis. 2008;14(2):308-10.

237. Maas R, Tacken M, Ruuls L, Koch G, van RE, Stockhofe-Zurwieden N. Avian influenza (H5N1) susceptibility and receptors in dogs. Emerg Infect Dis. 2007;13(8):1219-21.

238. Reperant LA, van AG, van de Bildt MW, Rimmelzwaan GF, Dobson AP, Osterhaus AD, Kuiken T. Highly pathogenic avian influenza virus (H5N1) infection in red foxes fed infected bird carcasses. Emerg Infect Dis. 2008;14(12):1835-41.

239. Kalthoff D, Hoffmann B, Harder T, Durban M, Beer M. Experimental infection of cattle with highly pathogenic avian influenza virus (H5N1). Emerg Infect Dis. 2008;14(7):1132-4.

240. Kim YI, Pascua PN, Kwon HI, Lim GJ, Kim EH, Yoon SW et al. Pathobiological features of a novel, highly pathogenic avian influenza A(H5N8) virus. Emerg Microbes Infect. 2014;3(10):e75.

241. Richard M, Herfst S, van den Brand JM, Lexmond P, Bestebroer TM, Rimmelzwaan GF, Koopmans M, Kuiken T, Fouchier RA. Low virulence and lack of airborne transmission of the Dutch highly pathogenic avian influenza virus H5N8 in ferrets. PLoS One. 2015;10(6):e0129827.

242. Pulit-Penaloza JA, Sun X, Creager HM, Zeng H, Belser JA, Maines TR, Tumpey TM. Pathogenesis and transmission of novel HPAI H5N2 and H5N8 avian influenza viruses in ferrets and mice. J Virol. 2015 [Epub ahead of print].

243. Ge FF, Zhou JP, Liu J, Wang J, Zhang WY, Sheng LP, Xu F, Ju HB, Sun QY, Liu PH. Genetic evolution of H9 subtype influenza viruses from live poultry markets in Shanghai, China. J Clin Microbiol. 2009;47(10):3294-300.

244. Zhang P, Tang Y, Liu X, Liu W, Zhang X, Liu H, Peng D, Gao S, Wu Y, Zhang L, Lu S, Liu X. A novel genotype H9N2 influenza virus possessing human H5N1 internal genomes has been circulating in poultry in eastern China since 1998. J Virol. 2009;83(17):8428-38.

245. Bi Y, Lu L, Li J, Yin Y, Zhang Y, Gao H, Qin Z, Zeshan B, Liu J, Sun L, Liu W. Novel genetic reassortants in H9N2 influenza A viruses and their diverse pathogenicity to mice. Virol J. 2011;8:505.

246. Fusaro A, Monne I, Salviato A, Valastro V, Schivo A, Amarin NM et al. Phylogeography and evolutionary history of reassortant H9N2 viruses with potential human health implications. J Virol. 2011;85(16):8413-21.

247. Dong G, Xu C, Wang C, Wu B, Luo J, Zhang H, Nolte DL, DeLiberto TJ, Duan M, Ji G, He H. Reassortant H9N2 influenza viruses containing H5N1-like PB1 genes isolated from black-billed magpies in Southern China. PLoS One. 2011;6(9):e25808.

248. Lindh E, Ek-Kommonen C, Vaananen VM, Vaheri A, Vapalahti O, Huovilainen A. Molecular epidemiology of H9N2 influenza viruses in Northern Europe. Vet Microbiol. 2014;172(3-4):548-54.

249. Body MH, Alrarawahi AH, Alhubsy SS, Saravanan N, Rajmony S, Mansoor MK. Characterization of low pathogenic avian influenza virus subtype H9N2 isolated from free-living Mynah birds (*Acridotheres tristis*) in the Sultanate of Oman. Avian Dis. 2015;59(2):329-34.

250. Vijaykrishna D, Smith GJ, Pybus OG, Zhu H, Bhatt S, Poon LL et al. Long-term evolution and transmission dynamics of swine influenza A virus. Nature. 2011;473(7348):519-22.

251. Zhou H, He SY, Sun L, He H, Ji F, Sun Y, Jia K, Ning Z, Wang H, Yuan L, Zhou P, Zhang G, Li S. Serological evidence of avian influenza virus and canine influenza virus infections among stray cats in live poultry markets, China. Vet Microbiol. 2015;175(2-4):369-73.

252. Amirsalehy H, Nili H, Mohammadi A. Can dogs carry the global pandemic candidate avian influenza virus H9N2? Aust Vet J. 2012;90(9):341-5.

253. Zhang K, Zhang Z, Yu Z, Li L, Cheng K, Wang T, Huang G, Yang S, Zhao Y, Feng N, Fu J, Qin C, Gao Y, Xia X. Domestic cats and dogs are susceptible to H9N2 avian influenza virus. Virus Res. 2013;175(1):52-7.

254. Karlsson EA, Engel GA, Feeroz MM, San S, Rompis A, Lee BP, Shaw E, Oh G, Schillaci MA, Grant R, Heidrich J, Schultz-Cherry S, Jones-Engel L. Influenza virus infection in nonhuman primates. Emerg Infect Dis. 2012;18(10):1672-5.

255. Yu H, Cowling BJ, Feng L, Lau EH, Liao Q, Tsang TK et al. Human infection with avian influenza A H7N9 virus: an assessment of clinical severity. Lancet. 2013;382(9887):138-45.

256. Liu T, Bi Z, Wang X, Li Z, Ding S, Bi Z et al. One family cluster of avian influenza A(H7N9) virus infection in Shandong, China. BMC Infect Dis. 2014;14:98.

257. Yang P, Pang X, Deng Y, Ma C, Zhang D, Sun Y et al. Surveillance for avian influenza A(H7N9), Beijing, China, 2013. Emerg Infect Dis. 2013;19(12):2041-3.

258. Meng Z, Han R, Hu Y, Yuan Z, Jiang S, Zhang X, Xu J. Possible pandemic threat from new reassortment of influenza A(H7N9) virus in China. Euro Surveill. 2014;19(6).

259. To KK, Chan JF, Chen H, Li L, Yuen KY. The emergence of influenza A H7N9 in human beings 16 years after influenza A H5N1: a tale of two cities. Lancet Infect Dis. 2013;13(9):809-21.

260. Lam TT, Wang J, Shen Y, Zhou B, Duan L, Cheung CL et al. The genesis and source of the H7N9 influenza viruses causing human infections in China. Nature. 2013;502(7470):241-4.

261. Lam TT, Zhou B, Wang J, Chai Y, Shen Y, Chen X et al. Dissemination, divergence and establishment of H7N9 influenza viruses in China. Nature. 2015;522(7554):102-5.

262. Zhao B, Zhang X, Zhu W, Teng Z, Yu X, Gao Y, Wu D, Pei E, Yuan Z, Yang L, Wang D, Shu Y, Wu F. Novel avian influenza A(H7N9) virus in tree sparrow, Shanghai, China, 2013. Emerg Infect Dis. 2014;20(5):850-3.

263. Ling F, Chen E, Liu Q, Miao Z, Gong Z. Hypothesis on the source, transmission and characteristics of infection of avian influenza A (H7N9) virus - based on analysis of field epidemiological investigation and gene sequence analysis. Zoonoses Public Health. 2015;62(1):29-37.

264. Lebarbenchon C, Brown JD, Stallknecht DE. Evolution of influenza A virus H7 and N9 subtypes, eastern Asia. Emerg Infect Dis. 2013;19(10):1635-8.

265. Pantin-Jackwood MJ, Miller PJ, Spackman E, Swayne DE, Susta L, Costa-Hurtado M, Suarez DL. Role of poultry in the spread of novel H7N9 influenza virus in China. J Virol. 2014;88(10):5381-90.

266. Jones JC, Sonnberg S, Kocer ZA, Shanmuganatham K, Seiler P, Shu Y, Zhu H, Guan Y, Peiris M, Webby RJ, Webster RG. Possible role of songbirds and parakeets in transmission of influenza A(H7N9) virus to humans. Emerg Infect Dis. 2014;20(3):380-5.

267. Liu Y, Yang Z, Wang X, Chen J, Yao J, Song Y, Lin J, Han C, Duan H, Zhao J, Pan J, Xie J. Pigeons are resistant to experimental infection with H7N9 avian influenza virus. Avian Pathol. 2015;44(5):342-6.

268. Watanabe T, Kiso M, Fukuyama S, Nakajima N, Imai M, Yamada S et al. Characterization of H7N9 influenza A viruses isolated from humans. Nature. 2013;501(7468):551-5.

269. Belser JA, Gustin KM, Pearce MB, Maines TR, Zeng H, Pappas C, Sun X, Carney PJ, Villanueva JM, Stevens J, Katz JM, Tumpey TM. Pathogenesis and transmission of avian influenza A (H7N9) virus in ferrets and mice. Nature. 2013;501(7468):556-9.

270. Xu L, Bao L, Deng W, Zhu H, Chen T, Lv Q et al. The mouse and ferret models for studying the novel avian-origin human influenza A (H7N9) virus. Virol J. 2013;10:253.

271. Zhou P, Hong M, Merrill MM, He H, Sun L, Zhang G. Serological report of influenza A (H7N9) infections among pigs in Southern China. BMC Vet Res. 2014;10(1):203.

272. Su S, Qi W, Chen J, Zhu W, Huang Z, Xie J, Zhang G. Seroepidemiological evidence of avian influenza A virus transmission to pigs in southern China. J Clin Microbiol. 2013;51(2):601-2.

273. Daly JM, Cullinane. Influenza infections [online]. In: Lekeux P, editor. Equine respiratory diseases. Ithaca NY: International Veterinary Information Service 189; 2013. Available at: http://www.ivis.org/special_books/Lekeux/daly/chapter.asp?LA=1. Accessed 16 June 2014.

274. Rooney, JR. Equine pathology. Ames, IA: Iowa State University Press; 1996. Influenza; p. 36-8.

275. Zhang C, Xuan Y, Shan H, Yang H, Wang J, Wang K, Li G, Qiao J. Avian influenza virus H9N2 infections in farmed minks. Virol J. 2015;12(1):180.

276. van Riel D, Rimmelzwaan GF, van Amerongen G, Osterhaus AD, 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(5):2185-90.

277. 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(1):39-45.

278. Hinshaw VS, Webster RG, Easterday BC, Bean WJ, Jr. Replication of avian influenza A viruses in mammals. Infect Immun. 1981;34(2):354-61.

279. Cheng K, Yu Z, Gao Y, Xia X, He H, Hua Y, Chai H. Experimental infection of dogs with H6N1 avian influenza A virus. Arch Virol. 2014;159(9):2275-82.

280. Su S, Qi W, Zhou P, Xiao C, Yan Z, Cui J, Jia K, Zhang G, Gray GC, Liao M, Li S. First evidence of H10N8 Avian influenza virus infections among feral dogs in live poultry markets in Guangdong province, China. Clin Infect Dis. 2014;59(5):748-50.

281. Leyva-Grado VH, Mubareka S, Krammer F, Cardenas WB, Palese P. Influenza virus infection in guinea pigs raised as livestock, Ecuador. Emerg Infect Dis. 2012;18(7):1135-8.

282. Hall JS, Bentler KT, Landolt G, Elmore SA, Minnis RB, Campbell TA, Barras SC, Root JJ, Pilon J, Pabilonia K, Driscoll C, Slate D, Sullivan H, McLean RG. Influenza infection in wild raccoons. Emerg Infect Dis. 2008;14(12):1842-8.

283. Roberts NM, Henzler DJ, Clark L. Serologic evidence of avian influenza (H4N6) exposure in a wild-caught raccoon. Avian Dis. 2009;53(3):455-7.

284. Root JJ, Shriner SA, Bentler KT, Gidlewski T, Mooers NL, Ellis JW, Spraker TR, VanDalen KK, Sullivan HJ, Franklin AB. Extended viral shedding of a low pathogenic avian influenza virus by striped skunks (*Mephitis mephitis*). PLoS One. 2014;9(1):e70639.

285. Root JJ, Shriner SA, Bentler KT, Gidlewski T, Mooers NL, Spraker TR, VanDalen KK, Sullivan HJ, Franklin AB. Shedding of a low pathogenic avian influenza virus in a common synanthropic mammal--the cottontail rabbit. PLoS One. 2014;9(8):e102513.

286. Bailey CF. Experimental infection of raccoon, skunk, and thirteen-lined ground squirrels with avian-derived influenza A viruses University of Minnesota; 1983..

287. White VC. A review of influenza viruses in seals and the implications for public health. US Army Med Dep J. 2013; 45-50.

288. Anthony SJ, St Leger JA, Pugliares K, Ip HS, Chan JM, Carpenter ZW et al. Emergence of fatal avian influenza in New England harbor seals. MBio. 2012;3(4):e00166-12.

289. Blanc A, Ruchansky D, Clara M, Achaval F, Le BA, Arbiza J. Serologic evidence of influenza A and B viruses in South American fur seals (*Arctocephalus australis*). J Wildl Dis. 2009;45(2):519-21.

290. Ohishi K, Ninomiya A, Kida H, Park CH, Maruyama T, Arai T, Katsumata E, Tobayama T, Boltunov AN, Khuraskin LS, Miyazaki N. Serological evidence of transmission of human influenza A and B viruses to Caspian seals (*Phoca caspica*). Microbiol Immunol. 2002;46(9):639-44.

291. Nielsen O, Clavijo A, Boughen JA. Serologic evidence of influenza A infection in marine mammals of Arctic Canada. J Wildl Dis. 2001;37(4):820-5.

292. Driskell EA, Jones CA, Stallknecht DE, Howerth EW, Tompkins SM. Avian influenza virus isolates from wild birds replicate and cause disease in a mouse model of infection. Virology. 2010;399(2):280-9.

293. Bui VN, Ogawa H, Xininigen, Karibe K, Matsuo K, Awad SS et al. H4N8 subtype avian influenza virus isolated from shorebirds contains a unique PB1 gene and causes severe respiratory disease in mice. Virology. 2012;423(1):77-88.

294. Nam JH, Kim EH, Song D, Choi YK, Kim JK, Poo H. Emergence of mammalian species-infectious and -pathogenic avian influenza H6N5 virus with no evidence of adaptation. J Virol. 2011;85(24):13271-7.

295. Driskell EA, Pickens JA, Humberd-Smith J, Gordy JT, Bradley KC, Steinhauer DA, Berghaus RD, Stallknecht DE, Howerth EW, Tompkins SM. Low pathogenic avian influenza isolates from wild birds replicate and transmit via contact in ferrets without prior adaptation. PLoS One. 2012;7(6):e38067.

296. Song H, Wan H, Araya Y, Perez DR. Partial direct contact transmission in ferrets of a mallard H7N3 influenza virus with typical avian-like receptor specificity. Virol J. 2009;14(6):126.

297. Marois P, Boudreault A, DiFranco E, Pavilanis V. Response of ferrets and monkeys to intranasal infection with human, equine and avian influenza viruses. Can J Comp Med. 1971;35(1):71-6.

298. Aamir UB, Naeem K, Ahmed Z, Obert CA, Franks J, Krauss S, Seiler P, Webster RG. Zoonotic potential of highly pathogenic avian H7N3 influenza viruses from Pakistan. Virology. 2009;390(2):212-20.
299. Gillim-Ross L, Santos C, Chen Z, Aspelund A, Yang CF, Ye D, Jin H, Kemble G, Subbarao K. Avian influenza H6 viruses productively infect and cause illness in mice and ferrets. J Virol. 2008;82(21):10854-63.
300. Belser JA, Lu X, Maines TR, Smith C, Li Y, Donis RO, Katz JM, Tumpey TM. Pathogenesis of avian influenza (H7) virus infection in mice and ferrets: enhanced virulence of Eurasian H7N7 viruses isolated from humans. J Virol. 2007;81(20):11139-47.
301. Shriner SA, VanDalen KK, Mooers NL, Ellis JW, Sullivan HJ, Root JJ, Pelzel AM, Franklin AB. Low-pathogenic avian influenza viruses in wild house mice. PLoS One. 2012;7(6):e39206.
302. Jin HK, Yamashita T, Ochiai K, Haller O, Watanabe T. Characterization and expression of the Mx1 gene in wild mouse species. Biochem Genet. 1998;36(9-10):311-22.
303. Tumpey TM, Szretter KJ, Van HN, Katz JM, Kochs G, Haller O, Garcia-Sastre A, Staeheli P. The Mx1 gene protects mice against the pandemic 1918 and highly lethal human H5N1 influenza viruses. J Virol. 2007;81(19):10818-21.
304. Nettles VF, Wood JM, Webster RG. Wildlife surveillance associated with an outbreak of lethal H5N2 avian influenza in domestic poultry. Avian Dis. 1985;29(3):733-41.
305. Henzler DJ, Kradel DC, Davison S, Ziegler AF, Singletary D, DeBok P, Castro AE, Lu H, Eckroade R, Swayne D, Lagoda W, Schmucker B, Nesselrodt A. Epidemiology, production losses, and control measures associated with an outbreak of avian influenza subtype H7N2 in Pennsylvania (1996-98). Avian Dis. 2003;47(3 Suppl):1022-36.
306. Shortridge KF, Gao P, Guan Y, Ito T, Kawaoka Y, Markwell D, Takada A, Webster RG. Interspecies transmission of influenza viruses: H5N1 virus and a Hong Kong SAR perspective. Vet Microbiol. 2000;74(1-2):141-7.
307. World Health Organization [WHO]. Cumulative number of confirmed human cases of avian influenza A/(H5N1) reported to WHO [online]. WHO;29 Aug 2013. Available at: http://www.who.int/influenza/human_animal_interface/H5N1_cumulative_table_archives/en/index.html. Accessed 27 Sept 2013.
308. Chen T, Zhang R. Symptoms seem to be mild in children infected with avian influenza A (H5N6) and other subtypes. J Infect. 2015 [Epub ahead of print].
309. Pan M, Gao R, Lv Q, Huang S, Zhou Z, Yang L et al. Human infection with a novel highly pathogenic avian influenza A (H5N6) virus: Virological and clinical findings. J Infect. 2015 [Epub ahead of print].
310. Yang ZF, Mok CK, Peiris JS, Zhong NS. Human infection with a novel avian influenza A(H5N6) virus. N Engl J Med. 2015;373(5):487-9.
311. Chen H, Yuan H, Gao R, Zhang J, Wang D, Xiong Y et al. Clinical and epidemiological characteristics of a fatal case of avian influenza A H10N8 virus infection: a descriptive study. Lancet. 2014;383(9918):714-21.
312. Wei SH, Yang JR, Wu HS, Chang MC, Lin JS, Lin CY et al. Human infection with avian influenza A H6N1 virus: an epidemiological analysis. Lancet Respir Med. 2013;1(10):771-8.
313. Ostrowsky B, Huang A, Terry W, Anton D, Brunagel B, Traynor L, Abid S, Johnson G, Kacica M, Katz J, Edwards L, Lindstrom S, Klimov A, Uyeki TM. Low pathogenic avian influenza A (H7N2) virus infection in immunocompromised adult, New York, USA, 2003. Emerg Infect Dis. 2012;18(7):1128-31.
314. Update: influenza activity--United States and worldwide, 2003-04 season, and composition of the 2004-05 influenza vaccine. MMWR Morb Mortal Wkly Rep. 2004;53(25):547-52.
315. Edwards LE, Terebuh P, Adija A, et al. Serological diagnosis of human infection with avian influenza A (H7N2) virus [Abstract 60, Session 44]. Presented at the International Conference on Emerging Infectious Diseases 2004, Atlanta, Georgia, February 22--March 3, 2004.
316. Fouchier RA, Schneeberger PM, Rozendaal FW, Broekman JM, Kemink SA, Munster V, Kuiken T, Rimmelzwaan GF, Schutten M, Van Doornum GJ, Koch G, Bosman A, Koopmans M, Osterhaus AD. Avian influenza A virus (H7N7) associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. Proc Natl Acad Sci U S A. 2004;101(5):1356-61.
317. Tweed SA, Skowronski DM, David ST, Larder A, Petric M, Lees W et al. Human illness from avian influenza H7N3, British Columbia. Emerg Infect Dis. 2004;10(12):2196-9.
318. Skowronski DM, Tweed SA, Petric M, Booth T, Li Y, Tam T. Human illness and isolation of low-pathogenicity avian influenza virus of the H7N3 subtype in British Columbia, Canada. J Infect Dis. 2006;193(6):899-900.
319. Eames KT, Webb C, Thomas K, Smith J, Salmon R, Temple JM. Assessing the role of contact tracing in a suspected H7N2 influenza A outbreak in humans in Wales. BMC Infect Dis. 2010;10:141.
320. Lopez-Martinez I, Balish A, Barrera-Badillo G, Jones J, Nunez-Garcia TE, Jang Y et al. Highly pathogenic avian influenza A(H7N3) virus in poultry workers, Mexico, 2012. Emerg Infect Dis. 2013;19(9).
321. Avian influenza A/(H7N2) outbreak in the United Kingdom. Euro Surveill. 2007;12(5):E070531.
322. Arzey GG, Kirkland PD, Arzey KE, Frost M, Maywood P, Conaty S, Hurt AC, Deng YM, Iannello P, Barr I, Dwyer DE, Ratnamohan M, McPhie K, Selleck P. Influenza virus A (H10N7) in chickens and poultry abattoir workers, Australia. Emerg Infect Dis. 2012;18(5):814-6.
323. Malik Peiris J. Avian influenza viruses in humans. Rev Sci Tech. 2008;28(1):161-74.
324. Peiris M, Yuen KY, Leung CW, Chan KH, Ip PL, Lai RW, Orr WK, Shortridge KF. Human infection with influenza H9N2. Lancet. 1999;354(9182):916-7.
325. Guo Y, Li J, Cheng X, Wang M, Zhou Y, Li C, et al. Discovery of men infected by avian influenza A (H9N2) virus. Chin J Exp Clin Virol. 1999;13:105e8.
326. Guo Y, Xie J, Wang M, Dang J, Guo J, Zhang Y, et al. A strain of influenza A H9N2 virus repeatedly isolated from human population in China. Chin J Exp Clin Virol. 2000;14:209e12.
327. Butt KM, Smith GJ, Chen H, Zhang LJ, Leung YH, Xu KM, Lim W, Webster RG, Yuen KY, Peiris JS, Guan Y. Human infection with an avian H9N2 influenza A virus in Hong Kong in 2003. J Clin Microbiol. 2005;43(11):5760-7.

328. ProMed Mail. PRO/AH/EDR> Avian influenza, human (124): H9N2 China (HK). Dec 24, 2009. Archive Number 20091224.4328. Available at http://www.promedmail.org. Accessed 28 Dec 2009.

329. Cheng VC, Chan JF, Wen X, Wu WL, Que TL, Chen H, Chan KH, Yuen KY. Infection of immunocompromised patients by avian H9N2 influenza A virus. J Infect. 2011;62(5):394-9.

330. Zhang W, Wan J, Qian K, Liu X, Xiao Z, Sun J et al. Clinical characteristics of human infection with a novel avian-origin influenza A(H10N8) virus. Chin Med J (Engl). 2014;127(18):3238-42.

331. Abdelwhab EM, Veits J, Mettenleiter TC. Prevalence and control of H7 avian influenza viruses in birds and humans. Epidemiol Infect. 2014;142(5):896-920.

332. Krueger WS, Khuntirat B, Yoon IK, Blair PJ, Chittagarnpitch M, Putnam SD, Supawat K, Gibbons RV, Bhuddari D, Pattamadilok S, Sawanpanyalert P, Heil GL, Gray GC. Prospective study of avian influenza virus infections among rural Thai villagers. PLoS One. 2013;8(8):e72196.

333. Chen Y, Zheng Q, Yang K, Zeng F, Lau SY, Wu WL, Huang S, Zhang J, Chen H, Xia N. Serological survey of antibodies to influenza A viruses in a group of people without a history of influenza vaccination. Clin Microbiol Infect. 2011;17(9):1347-9.

334. Khuntirat BP, Yoon IK, Blair PJ, Krueger WS, Chittaganpitch M, Putnam SD, Supawat K, Gibbons RV, Pattamadilok S, Sawanpanyalert P, Heil GL, Friary JA, Capuano AW, Gray GC. Evidence for subclinical avian influenza virus infections among rural Thai villagers. Clin Infect Dis. 2011;53(8):e107-e116.

335. Coman A, Maftei DN, Krueger WS, Heil GL, Friary JA, Chereches RM, Sirlincan E, Bria P, Dragnea C, Kasler I, Gray GC. Serological evidence for avian H9N2 influenza virus infections among Romanian agriculture workers. J Infect Public Health. 2013.

336. Okoye J, Eze D, Krueger WS, Heil GL, Friary JA, Gray GC. Serologic evidence of avian influenza virus infections among Nigerian agricultural workers. J Med Virol. 2013;85(4):670-6.

337. Uyeki TM, Nguyen DC, Rowe T, Lu X, Hu-Primmer J, Huynh LP, Hang NL, Katz JM. Seroprevalence of antibodies to avian influenza A (H5) and A (H9) viruses among market poultry workers, Hanoi, Vietnam, 2001. PLoS One. 2012;7(8):e43948.

338. Pawar S, Chakrabarti A, Cherian S, Pande S, Nanaware M, Raut S, Pal B, Jadhav S, Kode S, Koratkar S, Thite V, Mishra A. An avian influenza A(H11N1) virus from a wild aquatic bird revealing a unique Eurasian-American genetic reassortment. Virus Genes. 2010;41(1):14-22.

339. Gray GC, McCarthy T, Capuano AW, Setterquist SF, Alavanja MC, Lynch CF. Evidence for avian influenza A infections among Iowa's agricultural workers. Influenza Other Respir Viruses. 2008;2(2):61-9.

340. Gill JS, Webby R, Gilchrist MJ, Gray GC. Avian influenza among waterfowl hunters and wildlife professionals. Emerg Infect Dis. 2006;12:1284-6.

341. Jia N, de Vlas SJ, Liu YX, Zhang JS, Zhan L, Dang RL, Ma YH, Wang XJ, Liu T, Yang GP, Wen QL, Richardus JH, Lu S, Cao WC. Serological reports of human infections of H7 and H9 avian influenza viruses in northern China. J Clin Virol. 2009;44(3):225-9.

342. Kayali G, Ortiz EJ, Chorazy ML, Gray GC. Evidence of previous avian influenza infection among US turkey workers. Zoonoses Public Health. 2010;57(4):265-72.

343. Wang M, Fu CX, Zheng BJ. Antibodies against H5 and H9 avian influenza among poultry workers in China. N Engl J Med. 2009;360(24):2583-4.

344. Di Trani L, Porru S, Bonfanti L, Cordioli P, Cesana BM, Boni A, Di Carlo AS, Arici C, Donatelli I, Tomao P, Vonesch N, De Marco MA. Serosurvey against H5 and H7 avian influenza viruses in Italian poultry workers. Avian Dis. 2012;56(4 Suppl):1068-71.

345. Kayali G, Barbour E, Dbaibo G, Tabet C, Saade M, Shaib HA, deBeauchamp J, Webby RJ. Evidence of infection with H4 and H11 avian influenza viruses among Lebanese chicken growers. PLoS One. 2011;6(10):e26818.

346. Huo X, Zu R, Qi X, Qin Y, Li L, Tang F, Hu Z, Zhu F. Seroprevalence of avian influenza A (H5N1) virus among poultry workers in Jiangsu Province, China: an observational study. BMC Infect Dis. 2012;12:93.

347. Gray GC, Krueger WS, Chum C, Putnam SD, Wierzba TF, Heil GL, Anderson BD, Yasuda CY, Williams M, Kasper MR, Saphonn V, Blair PJ. Little evidence of subclinical avian influenza virus infections among rural villagers in Cambodia. PLoS One. 2014;9(5):e97097.

348. Komadina N, McVernon J, Hall R, Leder K. A historical perspective of influenza A(H1N2) virus. Emerg Infect Dis. 2014;20(1):6-12.

349. Xu KM, Smith GJ, Bahl J, Duan L, Tai H, Vijaykrishna D, Wang J, Zhang JX, Li KS, Fan XH, Webster RG, Chen H, Peiris JS, Guan Y. The genesis and evolution of H9N2 influenza viruses in poultry from southern China, 2000 to 2005. J Virol. 2007;81(19):10389-401.

350. Negovetich NJ, Feeroz MM, Jones-Engel L, Walker D, Alam SM, Hasan K et al. Live bird markets of Bangladesh: H9N2 viruses and the near absence of highly pathogenic H5N1 influenza. PLoS One. 2011;6(4):e19311.

351. Monne I, Hussein HA, Fusaro A, Valastro V, Hamoud MM, Khalefa RA, Dardir SN, Radwan MI, Capua I, Cattoli G. H9N2 influenza A virus circulates in H5N1 endemically infected poultry population in Egypt. Influenza Other Respir Viruses. 2013;7(3):240-3.

352. Nili H, Asasi K. Natural cases and an experimental study of H9N2 avian influenza in commercial broiler chickens of Iran. Avian Pathol. 2002;31:247-52.

353. Baumer A, Feldmann J, Renzullo S, Muller M, Thur B, Hofmann MA. Epidemiology of avian influenza virus in wild birds in Switzerland between 2006 and 2009. Avian Dis. 2010;54(2):875-84.

354. Globig A, Baumer A, Revilla-Fernandez S, Beer M, Wodak E, Fink M et al. Ducks as sentinels for avian influenza in wild birds. Emerg Infect Dis. 2009;15(10):1633-6.

355. Lin PH, Chao TL, Kuo SW, Wang JT, Hung CC, Lin HC et al. Virological, serological, and antiviral studies in an imported human case of avian influenza A(H7N9) virus in Taiwan. Clin Infect Dis. 2014;58(2):242-6.

356. To KK, Song W, Lau SY, Que TL, Lung DC, Hung IF, Chen H, Yuen KY. Unique reassortant of influenza A(H7N9) virus associated with severe disease emerging in Hong Kong. J Infect. 2014.

357. Gilbert M, Jambal L, Karesh WB, Fine A, Shiilegdamba E, Dulam P et al. Highly pathogenic avian influenza virus among wild birds in Mongolia. PLoS One. 2012;7(9):e44097.

358. Sharshov K, Silko N, Sousloparov I, Zaykovskaya A, Shestopalov A, Drozdov I. Avian influenza (H5N1) outbreak among wild birds, Russia, 2009. Emerg Infect Dis. 2010;16(2):349-51.

359. Dusek RJ, Bortner JB, DeLiberto TJ, Hoskins J, Franson JC, Bales BD, Yparraguirre D, Swafford SR, Ip HS. Surveillance for high pathogenicity avian influenza virus in wild birds in the Pacific Flyway of the United States, 2006-2007. Avian Dis. 2009;53(2):222-30.

360. Langstaff IG, McKenzie JS, Stanislawek WL, Reed CE, Poland R, Cork SC. Surveillance for highly pathogenic avian influenza in migratory shorebirds at the terminus of the East Asian-Australasian Flyway. N Z Vet J. 2009;57(3):160-5.

361. Sims LD. Progress in control of H5N1 highly pathogenic avian influenza and the future for eradication. Avian Dis. 2012;56(4 Suppl):829-35.

362. Tumpey TM, Kapczynski DR, Swayne DE. Comparative susceptibility of chickens and turkeys to avian influenza A H7N2 virus infection and protective efficacy of a commercial avian influenza H7N2 virus vaccine. Avian Dis. 2004;48(1):167-76.

363. Killian ML. Avian influenza virus sample types, collection, and handling. Methods Mol Biol. 2014;1161:83-91.

364. Hofle U, van de Bildt MW, Leijten LM, van AG, Verhagen JH, Fouchier RA, Osterhaus AD, Kuiken T. Tissue tropism and pathology of natural influenza virus infection in black-headed gulls (*Chroicocephalus ridibundus*). Avian Pathol. 2012;41(6):547-53.

365. Magor KE. Immunoglobulin genetics and antibody responses to influenza in ducks. Dev Comp Immunol. 2011;35(9):1008-16.

366. Pantin-Jackwood MJ, Suarez DL. Vaccination of domestic ducks against H5N1 HPAI: a review. Virus Res. 2013;178(1):21-34.

367. Antarasena C, Sirimujalin R, Prommuang P, Blacksell SD, Promkuntod N, Prommuang P. Tissue tropism of a Thailand strain of high-pathogenicity avian influenza virus (H5N1) in tissues of naturally infected native chickens (*Gallus gallus*), Japanese quail (*Coturnix coturnix japonica*) and ducks (*Anas spp*.). Avian Pathol. 2006;35(3):250-3.

368. Krauss S, Pryor SP, Raven G, Danner A, Kayali G, Webby RJ, Webster RG. Respiratory tract versus cloacal sampling of migratory ducks for influenza A viruses: are both ends relevant? Influenza Other Respi Viruses. 2013;7(1):93-6.

369. Wanaratana S, Panyim S, Pakpinyo S. The potential of house flies to act as a vector of avian influenza subtype H5N1 under experimental conditions. Med Vet Entomol. 2011;25(1):58-63.

370. Nielsen AA, Skovgard H, Stockmarr A, Handberg KJ, Jorgensen PH. Persistence of low-pathogenic avian influenza H5N7 and H7N1 subtypes in house flies (Diptera: Muscidae). J Med Entomol. 2011;48(3):608-14.

371. Ypma RJ, Jonges M, Bataille A, Stegeman A, Koch G, van Boven M, Koopmans M, van Ballegooijen WM, Wallinga J. Genetic data provide evidence for wind-mediated transmission of highly pathogenic avian influenza. J Infect Dis. 2013;207(5):730-5.

372. Cappucci DT, Johnson DC, Brugh M, Smith TM, Jackson CF, Pearson JE, Senne DA. Isolation of avian influenza virus (subtype H5N2) from chicken eggs during a natural outbreak. Avian Dis. 1985;29:1195-200.

373. Moses HE, Brandley CA, Jones EE. The isolation and identification of fowl plague virus. Am J Vet Res. 1948;9:314-28.

374. Promkuntod N, Antarasena C, Prommuang P, Prommuang P. Isolation of avian influenza virus A subtype H5N1 from internal contents (albumen and allantoic fluid) of Japanese quail (*Coturnix coturnix japonica*) eggs and oviduct during a natural outbreak. Ann N Y Acad Sci. 2006;1081:171-3.

375. Beard CW, Brugh M, Johnson DC. Laboratory studies with the Pennsylvania avian influenza viruses (H5N2). 1984 p. 462-73.

376. Bean WJ, Kawaoka Y, Wood JM, Pearson JE, Webster RG. Characterization of virulent and avirulent A/chicken/Pennsylvania/83 influenza A viruses: potential role of defective interfering RNAs in nature. J Virol. 1985;54(1):151-60.

377. Narayan O, Lang G, Rouse BT. A new influenza A virus infection in turkeys. IV. Experimental susceptibility of domestic birds to virus strain turkey-Ontario 7732-1966. Arch Gesamte Virusforsch. 1969;26(1):149-65.

378. Kilany WH, Arafa A, Erfan AM, Ahmed MS, Nawar AA, Selim AA, Khoulosy SG, Hassan MK, Aly MM, Hafez HM, Abdelwhab EM. Isolation of highly pathogenic avian influenza H5N1 from table eggs after vaccinal break in commercial layer flock. Avian Dis. 2010;54(3):1115-9.

379. Spickler AR, Trampel DW, Roth JA. The onset of virus shedding and clinical signs in chickens infected with high-pathogenicity and low-pathogenicity avian influenza viruses. Avian Pathol. 2008;37:555-77.

380. Stallknecht DE, Brown JD. Tenacity of avian influenza viruses. Rev Sci Tech. 2009;28(1):59-67.

381. Lu H, Castro AE, Pennick K, Liu J, Yang Q, Dunn P, Weinstock D, Henzler D. Survival of avian influenza virus H7N2 in SPF chickens and their environments. Avian Dis. 2003;47(3 Suppl):1015-21.

382. Humberd J, Guan Y, Webster RG. Comparison of the replication of influenza A viruses in Chinese ring-necked pheasants and chukar partridges. J Virol. 2006;80(5):2151-61.

383. Shi J, Xie J, He Z, Hu Y, He Y, Huang Q, Leng B, He W, Sheng Y, Li F, Song Y, Bai C, Gu Y, Jie Z. A detailed epidemiological and clinical description of 6 human cases of avian-origin influenza A (H7N9) virus infection in Shanghai. PLoS One. 2013;8(10):e77651.

384. Cowling BJ, Jin L, Lau EH, Liao Q, Wu P, Jiang H et al. Comparative epidemiology of human infections with avian influenza A H7N9 and H5N1 viruses in China: a population-based study of laboratory-confirmed cases. Lancet. 2013.

385. Murhekar M, Arima Y, Horby P, Vandemaele KA, Vong S, Zijian F, Lee CK, Li A. Avian influenza A(H7N9) and the closure of live bird markets. Western Pac Surveill Response J. 2013;4(2):4-7.

386. Zhang J, Geng X, Ma Y, Ruan S, Xu S, Liu L, Xu H, Yang G, Wang C, Liu C, Han X, Yu Q, Cheng H, Li Z. Fatal avian influenza (H5N1) infection in human, China. Emerg Infect Dis. 2010;16(11):1799-801.

387. Ungchusak K, Auewarakul P, Dowell SF, Kitphati R, Auwanit W, Puthavathana P et al. Probable person-to-person transmission of avian influenza A (H5N1). N Engl J Med. 2005;352(4):333-40.

388. Liao Q, Bai T, Zhou L, Vong S, Guo J, Lv W et al. Seroprevalence of antibodies to highly pathogenic avian influenza A (H5N1) virus among close contacts exposed to H5N1 cases, China, 2005-2008. PLoS One. 2013;8(8):e71765.

389. Human cases of avian influenza A (H5N1) in North-West Frontier Province, Pakistan, October-November 2007. Wkly Epidemiol Rec. 2008;83(40):359-64.

390. Wang H, Feng Z, Shu Y, Yu H, Zhou L, Zu R et al. Probable limited person-to-person transmission of highly pathogenic avian influenza A (H5N1) virus in China. Lancet. 2008;371(9622):1427-34.

391. Lipatov AS, Kwon YK, Pantin-Jackwood MJ, Swayne DE. Pathogenesis of H5N1 influenza virus infections in mice and ferret models differs according to respiratory tract or digestive system exposure. J Infect Dis. 2009;199(5):717-25.

392. ProMed Mail. PRO/AH/EDR> Avian influenza, human - Thailand (06). Sept. 9, 2004. Archive Number 20040909.2513. Available at http://www.promedmail.org. Accessed 8 Dec 2009

393. Vong S, Ly S, Van Kerkhove MD, Achenbach J, Holl D, Buchy P, Sorn S, Seng H, Uyeki TM, Sok T, Katz JM. Risk factors associated with subclinical human infection with avian influenza A (H5N1) virus--Cambodia, 2006. J Infect Dis. 2009;199(12):1744-52.

394. Belser JA, Wadford DA, Xu J, Katz JM, Tumpey TM. Ocular infection of mice with influenza A (H7) viruses: a site of primary replication and spread to the respiratory tract. J Virol. 2009;83(14):7075-84.

395. Bischoff WE, Reid T, Russell GB, Peters TR. Transocular entry of seasonal influenza-attenuated virus aerosols and the efficacy of n95 respirators, surgical masks, and eye protection in humans. J Infect Dis. 2011;204(2):193-9.

396. Vahlenkamp TW, Teifke JP, Harder TC, Beer M, Mettenleiter TC. Systemic influenza virus H5N1 infection in cats after gastrointestinal exposure. Influenza Other Respi Viruses. 2010;4(6):379-86.

397. Shinya K, Makino A, Tanaka H, Hatta M, Watanabe T, Le MQ, Imai H, Kawaoka Y. Systemic dissemination of H5N1 influenza A viruses in ferrets and hamsters after direct intragastric inoculation. J Virol. 2011;85(10):4673-8.

398. Sweet C, Smith H. Pathogenicity of influenza virus. Microbiol Rev. 1980;44(2):303-30.

399. Gu J, Xie Z, Gao Z, Liu J, Korteweg C, Ye J et al. H5N1 infection of the respiratory tract and beyond: a molecular pathology study. Lancet. 2007;370:1137-45.

400. Dilantika C, Sedyaningsih ER, Kasper MR, Agtini M, Listiyaningsih E, Uyeki TM, Burgess TH, Blair PJ, Putnam SD. Influenza virus infection among pediatric patients reporting diarrhea and influenza-like illness. BMC Infect Dis. 2010;10:3.

401. Chan MC, Lee N, Chan PK, To KF, Wong RY, Ho WS, Ngai KL, Sung JJ. Seasonal influenza A virus in feces of hospitalized adults. Emerg Infect Dis. 2011;17(11):2038-42.

402. de Jong MD, Bach VC, Phan TQ, Vo MH, Tran TT, Nguyen BH, Beld M, Le TP, Truong HK, Nguyen VV, Tran TH, Do QH, Farrar J. Fatal avian influenza A (H5N1) in a child presenting with diarrhea followed by coma. N Engl J Med. 2005;352(7):686-91.

403. Buchy P, Mardy S, Vong S, Toyoda T, Aubin JT, Miller M et al. Influenza A/H5N1 virus infection in humans in Cambodia. J Clin Virol. 2007;39(3):164-8.

404. Song R, Pang X, Yang P, Shu Y, Zhang Y, Wang Q et al. Surveillance of the first case of human avian influenza A (H7N9) virus in Beijing, China. Infection. 2014;42(1):127-33.

405. Yu L, Wang Z, Chen Y, Ding W, Jia H, Chan JF et al. Clinical, virological, and histopathological manifestations of fatal human infections by avian influenza A(H7N9) virus. Clin Infect Dis. 2013;57(10):1449-57.

406. Shu Y, Li CK, Li Z, Gao R, Liang Q, Zhang Y et al. Avian influenza A(H5N1) viruses can directly infect and replicate in human gut tissues. J Infect Dis. 2010;201(8):1173-7.

407. Goldstein T, Mena I, Anthony SJ, Medina R, Robinson PW, Greig DJ, Costa DP, Lipkin WI, Garcia-Sastre A, Boyce WM. Pandemic H1N1 influenza isolated from free-ranging Northern Elephant Seals in 2010 off the central California coast. PLoS One. 2013;8(5):e62259.

408. Abbott A. Human fatality adds fresh impetus to fight against bird flu. Nature. 2003;423(6935):5.

409. Hsieh SM, Huang YS, Chang SY, Lin PH, Chang SC. Serological survey in close contacts with a confirmed case of H7N9 influenza in Taiwan. J Infect. 2013;67(5):494-5.

410. Li Q, Zhou L, Zhou M, Chen Z, Li F, Wu H et al. Epidemiology of human infections with avian influenza A(H7N9) virus in China. N Engl J Med. 2014;370(6):520-32.

411. Qi X, Qian YH, Bao CJ, Guo XL, Cui LB, Tang FY et al. Probable person to person transmission of novel avian influenza A (H7N9) virus in eastern China, 2013: epidemiological investigation. BMJ. 2013;347:f4752.

412. Hu J, Zhu Y, Zhao B, Li J, Liu L, Gu K, Zhang W, Su H, Teng Z, Tang S, Yuan Z, Feng Z, Wu F. Limited human-to-human transmission of avian influenza A(H7N9) virus, Shanghai, China, March to April 2013. Euro Surveill. 2014;19(25).

413. Xiao XC, Li KB, Chen ZQ, DI B, Yang ZC, Yuan J, Luo HB, Ye SL, Liu H, Lu JY, Nie Z, Tang XP, Wang M, Zheng BJ. Transmission of avian influenza A(H7N9) virus from father to child: a report of limited person-to-person transmission, Guangzhou, China, January 2014. Euro Surveill. 2014;19(25).

414. Fang CF, Ma MJ, Zhan BD, Lai SM, Hu Y, Yang XX et al. Nosocomial transmission of avian influenza A (H7N9) virus in China: epidemiological investigation. BMJ. 2015;351:h5765.

415. Nidom CA, Takano R, Yamada S, Sakai-Tagawa Y, Daulay S, Aswadi D, Suzuki T, Suzuki Y, Shinya K, Iwatsuki-Horimoto K, Muramoto Y, Kawaoka Y. Influenza A (H5N1) viruses from pigs, Indonesia. Emerg Infect Dis. 2010;16(10):1515-23.

416. Hu X, Liu D, Wang M, Yang L, Wang M, Zhu Q, Li L, Gao GF. Clade 2.3.2 avian influenza virus (H5N1), Qinghai Lake region, China, 2009-2010. Emerg Infect Dis. 2011;17(3):560-2.
417. De Benedictis P., Beato MS, Capua I. Inactivation of avian influenza viruses by chemical agents and physical conditions: a review. Zoonoses Public Health. 2007;54(2):51-68.
418. Brown JD, Swayne DE, Cooper RJ, Burns RE, Stallknecht DE. Persistence of H5 and H7 avian influenza viruses in water. Avian Dis. 2007;51(1 Suppl):285-9.
419. Beato MS, Mancin M, Bertoli E, Buratin A, Terregino C, Capua I. Infectivity of H7 LP and HP influenza viruses at different temperatures and pH and persistence of H7 HP virus in poultry meat at refrigeration temperature. Virology. 2012;433(2):522-7.
420. Davidson I, Nagar S, Haddas R, Ben-Shabat M, Golender N, Lapin E, Altory A, Simanov L, Ribshtein I, Panshin A, Perk S. Avian influenza virus H9N2 survival at different temperatures and pHs. Avian Dis. 2010;54(1 Suppl):725-8.
421. Nielsen AA, Jensen TH, Stockmarr A, Jorgensen PH. Persistence of low-pathogenic H5N7 and H7N1 avian influenza subtypes in filtered natural waters. Vet Microbiol. 2013;166(3-4):419-28.
422. Domanska-Blicharz K, Minta Z, Smietanka K, Marche S, van den Berg T. H5N1 high pathogenicity avian influenza virus survival in different types of water. Avian Dis. 2010;54(1 Suppl):734-7.
423. Nazir J, Haumacher R, Ike A, Stumpf P, Bohm R, Marschang RE. Long-term study on tenacity of avian influenza viruses in water (distilled water, normal saline, and surface water) at different temperatures. Avian Dis. 2010;54(1 Suppl):720-4.
424. Wood JP, Choi YW, Chappie DJ, Rogers JV, Kaye JZ. Environmental persistence of a highly pathogenic avian influenza (H5N1) virus. Environ Sci Technol. 2010;44(19):7515-20.
425. Stallknecht DE, Goekjian VH, Wilcox BR, Poulson RL, Brown JD. Avian influenza virus in aquatic habitats: what do we need to learn? Avian Dis. 2010;54(1 Suppl):461-5.
426. Webster RG, Yakhno M, Hinshaw VS, Bean WJ, Murti KG. Intestinal influenza: replication and characterization of influenza viruses in ducks. Virology. 1978;84(2):268-78.
427. Brown JD, Goekjian G, Poulson R, Valeika S, Stallknecht DE. Avian influenza virus in water: infectivity is dependent on pH, salinity and temperature. Vet Microbiol. 2009;136(1-2):20-6.
428. Songserm T, Jam-On R, Sae-Heng N, Meemak N. Survival and stability of HPAI H5N1 in different environments and susceptibility to disinfectants. Dev Biol (Basel). 2006;124:254.
429. Paek MR, Lee YJ, Yoon H, Kang HM, Kim MC, Choi JG, Jeong OM, Kwon JS, Moon OK, Lee SJ, Kwon JH. Survival rate of H5N1 highly pathogenic avian influenza viruses at different temperatures. Poult Sci. 2010;89(8):1647-50.
430. Terregino C, Beato MS, Bertoli E, Mancin M, Capua I. Unexpected heat resistance of Italian low-pathogenicity and high-pathogenicity avian influenza A viruses of H7 subtype to prolonged exposure at 37 degrees C. Avian Pathol. 2009;38(6):519-22.
431. Brown J, Stallknecht D, Lebarbenchon C, Swayne D. Survivability of Eurasian H5N1 highly pathogenic avian influenza viruses in water varies between strains. Avian Dis. 2014;58(3):453-7.
432. Shortridge KF, Zhou NN, Guan Y, Gao P, Ito T, Kawaoka Y et al. Characterization of avian H5N1 influenza viruses from poultry in Hong Kong. Virology. 1998;252(2):331-42.
433. Yamamoto Y, Nakamura K, Yamada M, Mase M. Persistence of avian influenza virus (H5N1) in feathers detached from bodies of infected domestic ducks. Appl Environ Microbiol. 2010;76(16):5496-9.
434. Nazir J, Haumacher R, Ike AC, Marschang RE. Persistence of avian influenza viruses in lake sediment, duck feces, and duck meat. Appl Environ Microbiol. 2011;77(14):4981-5.
435. Horm VS, Gutierrez RA, Nicholls JM, Buchy P. Highly pathogenic influenza A(H5N1) virus survival in complex artificial aquatic biotopes. PLoS One. 2012;7(4):e34160.
436. Chumpolbanchorn K, Suemanotham N, Siripara N, Puyati B, Chaichoune K. The effect of temperature and UV light on infectivity of avian influenza virus (H5N1, Thai field strain) in chicken fecal manure. Southeast Asian J Trop Med Public Health. 2006;37(1):102-5.
437. Tiwari A, Patnayak DP, Chander Y, Parsad M, Goyal SM. Survival of two avian respiratory viruses on porous and nonporous surfaces. Avian Dis. 2006;50(2):284-7.
438. Horm SV, Gutierrez RA, Sorn S, Buchy P. Environment: a potential source of animal and human infection with influenza A (H5N1) virus. Influenza Other Respi Viruses. 2012;6(6):442-8.
439. International Committee on Taxonomy of Viruses 133. Universal virus database, version 3. 00.046. Orthomyxoviridae [online]. ICTV; 2003. Available at: http://www.ncbi.nlm.nih.gov/ICTVdb/ICTVdB. Accessed 15 Dec 2009.
440. Public Health Agency of Canada. Pathogen Safety Data Sheet – Influenza A virus type A. Pathogen Regulation Directorate, Public Health Agency of Canada; 2012 Feb. Available at: http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/influenza-a-eng.php. Accessed 16 June 2014.
441. Public Health Agency of Canada. Pathogen Safety Data Sheet – Influenza A virus subtypes H5, H7 and H9. Pathogen Regulation Directorate, Public Health Agency of Canada; 2012 Apr. Available at: http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/influenza-grippe-a-eng.php. Accessed 16 June 2014
442. Ardans AA. Equine influenza. In: Hirsch DC, Zee YC, editors. Veterinary microbiology. Malden, MA: Blackwell Science; 1999. p. 398-399.
443. Johnson DC, Maxfield BG. An occurrence of avian influenza virus infection in laying chickens. Avian Dis. 1976;20(2):422-4.
444. Alexander DJ, Stuart JC. Isolation of an influenza A virus from domestic fowl in Great Britain. Vet Rec. 1982;111(18):416.
445. Hooper PT, Russell GW, Selleck PW, Stanislawek WL. Observations on the relationship in chickens between the virulence of some avian influenza viruses and their pathogenicity for various organs. Avian Dis. 1995;39(3):458-64.

446. Ziegler AF, Davison S, Acland H, Eckroade RJ. Characteristics of H7N2 (nonpathogenic) avian influenza virus infections in commercial layers, in Pennsylvania, 1997-98. Avian Dis. 1999;43(1):142-9.

447. Kinde H, Read DH, Daft BM, Hammarlund M, Moore J, Uzal F, Mukai J, Woolcock P. The occurrence of avian influenza A subtype H6N2 in commercial layer flocks in Southern California (2000-02): clinicopathologic findings. Avian Dis. 2003;47(3 Suppl):1214-8.

448. Mutinelli F, Capua I, Terregino C, Cattoli G. Clinical, gross, and microscopic findings in different avian species naturally infected during the H7N1 low- and high-pathogenicity avian influenza epidemics in Italy during 1999 and 2000. Avian Dis. 2003;47(3 Suppl):844-8.

449. Nili H, Asasi K. Avian influenza (H9N2) outbreak in Iran. Avian Dis. 2003;47(3 Suppl):828-31.

450. Bowes VA, Ritchie SJ, Byrne S, Sojonky K, Bidulka JJ, Robinson JH. Virus characterization, clinical presentation, and pathology associated with H7N3 avian influenza in British Columbia broiler breeder chickens in 2004. Avian Dis. 2004;48(4):928-34.

451. Lu H, Castro AE. Evaluation of the infectivity, length of infection, and immune response of a low-pathogenicity H7N2 avian influenza virus in specific-pathogen-free chickens. Avian Dis. 2004;48(2):263-70.

452. Bertran K, Dolz R, Majo N. Pathobiology of avian influenza virus infection in minor gallinaceous species: a review. Avian Pathol. 2014;43(1):9-25.

453. Jourdain E, Gunnarsson G, Wahlgren J, Latorre-Margalef N, Brojer C, Sahlin S, Svensson L, Waldenstrom J, Lundkvist A, Olsen B. Influenza virus in a natural host, the mallard: experimental infection data. PLoS One. 2010;5(1):e8935.

454. van Gils JA, Munster VJ, Radersma R, Liefhebber D, Fouchier RA, Klaassen M. Hampered foraging and migratory performance in swans infected with low-pathogenic avian influenza A virus. PLoS One. 2007;2(1):e184.

455. Iqbal M, Yaqub T, Mukhtar N, Shabbir MZ, McCauley JW. Infectivity and transmissibility of H9N2 avian influenza virus in chickens and wild terrestrial birds. Vet Res. 2013;44:100.

456. Pazani J, Marandi MV, Ashrafihelan J, Marjanmehr SH, Ghods F. Pathological studies of A/Chicken/Tehran/ZMT-173/99 (H9N2) influenza virus in commercial broiler chickens of Iran. Int J Poultry Sci. 2008;7:502-10.

457. Ebrahimi SM, Ziapour S, Tebianian M, Dabaghian M, Mohammadi M. Study of infection with an Iranian field-isolated H9N2 avian influenza virus in vaccinated and unvaccinated Japanese quail. Avian Dis. 2011;55(2):195-200.

458. Forman AJ, Parsonson IM, Doughty WJ. The pathogenicity of an avian influenza virus isolated in Victoria. Aust Vet J. 1986;63(9):294-6.

459. Elbers AR, Fabri TH, de Vries TS, de Wit JJ, Pijpers A, Koch G. The highly pathogenic avian influenza A (H7N7) virus epidemic in The Netherlands in 2003--lessons learned from the first five outbreaks. Avian Dis. 2004;48(3):691-705.

460. Nakatani H, Nakamura K, Yamamoto Y, Yamada M, Yamamoto Y. Epidemiology, pathology, and immunohistochemistry of layer hens naturally affected with H5N1 highly pathogenic avian influenza in Japan. Avian Dis. 2005;49(3):436-41.

461. Tsukamoto K, Imada T, Tanimura N, Okamatsu M, Mase M, Mizuhara T, Swayne D, Yamaguchi S. Impact of different husbandry conditions on contact and airborne transmission of H5N1 highly pathogenic avian influenza virus to chickens. Avian Dis. 2007;51(1):129-32.

462. Beard CW. Avian influenza. Foreign animal diseases.Richmond, VA: United States Animal Health Association; 1998. p. 71-80.

463. Capua I, Mutinelli F. Mortality in Muscovy ducks (*Cairina moschata*) and domestic geese (*Anser anser* var. *domestica*) associated with natural infection with a highly pathogenic avian influenza virus of H7N1 subtype. Avian Pathol. 2001;30(2):179-83.

464. Yamamoto Y, Nakamura K, Yamada M, Mase M. Corneal opacity in domestic ducks experimentally infected with H5N1 highly pathogenic avian influenza virus. Vet Pathol. 2015. [Epub ahead of print]

465. Mansour SM, ElBakrey RM, Ali H, Knudsen DE, Eid AA. Natural infection with highly pathogenic avian influenza virus H5N1 in domestic pigeons (*Columba livia*) in Egypt. Avian Pathol. 2014;43(4):319-24.

466. Kalthoff D, Breithaupt A, Teifke JP, Globig A, Harder T, Mettenleiter TC, Beer M. Highly pathogenic avian influenza virus (H5N1) in experimentally infected adult mute swans. Emerg Infect Dis. 2008;14(8):1267-70.

467. Keawcharoen J, van RD, van AG, Bestebroer T, Beyer WE, van LR, Osterhaus AD, Fouchier RA, Kuiken T. Wild ducks as long-distance vectors of highly pathogenic avian influenza virus (H5N1). Emerg Infect Dis. 2008;14(4):600-7.

468. Komar N, Olsen B. Avian influenza virus (H5N1) mortality surveillance. Emerg Infect Dis. 2008;14(7):1176-8.

469. Ramis A, van Amerongen G, van de Bildt M, Leijten L, Vanderstichel R, Osterhaus A, Kuiken T. Experimental infection of highly pathogenic avian influenza virus H5N1 in black-headed gulls (. Vet Res. 2014;45(1):84.

470. van den Brand JM, Krone O, Wolf PU, van de Bildt MW, van AG, Osterhaus AD, Kuiken T. Host-specific exposure and fatal neurologic disease in wild raptors from highly pathogenic avian influenza virus H5N1 during the 2006 outbreak in Germany. Vet Res. 2015;46:24.

471. Hall JS, Ip HS, Franson JC, Meteyer C, Nashold S, TeSlaa JL, French J, Redig P, Brand C. Experimental infection of a North American raptor, American Kestrel (*Falco sparverius*), with highly pathogenic avian influenza virus (H5N1). PLoS One. 2009;4(10):e7555.

472. Marinova-Petkova A, Georgiev G, Seiler P, Darnell D, Franks J, Krauss S, Webby RJ, Webster RG. Spread of influenza virus A (H5N1) clade 2.3.2.1 to Bulgaria in common buzzards. Emerg Infect Dis. 2012;18(10):1596-602.

473. Shivakoti S, Ito H, Otsuki K, Ito T. Characterization of H5N1 highly pathogenic avian influenza virus isolated from a mountain hawk eagle in Japan. J Vet Med Sci. 2010;72(4):459-63.

474. Naguib MM, Kinne J, Chen H, Chan KH, Joseph S, Wong PC, Woo PC, Wernery R, Beer M, Wernery U, Harder TC. Outbreaks of highly pathogenic avian influenza H5N1 clade 2.3.2.1c in hunting falcons and kept wild birds in Dubai implicate intercontinental virus spread. J Gen Virol. 2015 [Epub ahead of print].

475. Fujimoto Y, Usui T, Ito H, Ono E, Ito T. Susceptibility of wild passerines to subtype H5N1 highly pathogenic avian influenza viruses. Avian Pathol. 2015;44(4):243-7.

476. Jeong J, Kang HM, Lee EK, Song BM, Kwon YK, Kim HR et al. Highly pathogenic avian influenza virus (H5N8) in domestic poultry and its relationship with migratory birds in South Korea during 2014. Vet Microbiol. 2014;173(3-4):249-57.

477. Kang HM, Lee EK, Song BM, Jeong J, Choi JG, Jeong J, Moon OK, Yoon H, Cho Y, Kang YM, Lee HS, Lee YJ. Novel reassortant influenza A(H5N8) viruses among inoculated domestic and wild ducks, South Korea, 2014. Emerg Infect Dis. 2015;21(2):298-304.

478. 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(1):305-13.

479. Stoskopf MK. Viral diseases of marine mammals: Influenza virus. In: Aiello SE, Moses MA. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2012. Marine mammals: Influenza virus. Available at: http://www.merckmanuals.com/vet/exotic_and_laboratory_animals/marine_mammals/viral_diseases_of_marine_mammals.html. Accessed 16 Jun 2014.

480. Groth M, Lange J, Kanrai P, Pleschka S, Scholtissek C, Krumbholz A, Platzer M, Sauerbrei A, Zell R. The genome of an influenza virus from a pilot whale: Relation to influenza viruses of gulls and marine mammals. Infect Genet Evol. 2014.

481. Lvov DK, Zdanov VM, Sazonov AA, Braude NA, Vladimirtceva EA, Agafonova LV et al. Comparison of influenza viruses isolated from man and from whales. Bull World Health Organ. 1978;56(6):923-30.

482. Elbers AR, Kamps B, Koch G. Performance of gross lesions at postmortem for the detection of outbreaks during the avian influenza A virus (H7N7) epidemic in The Netherlands in 2003. Avian Pathol. 2004;33(4):418-22.

483. Ogawa S, Yamamoto Y, Yamada M, Mase M, Nakamura K. Pathology of whooper swans (*Cygnus cygnus*) infected with H5N1 avian influenza virus in Akita, Japan, in 2008. J Vet Med Sci. 2009;71(10):1377-80.

484. Nuradji H, Bingham J, Lowther S, Wibawa H, Colling A, Long NT, Meers J. A comparative evaluation of feathers, oropharyngeal swabs, and cloacal swabs for the detection of H5N1 highly pathogenic avian influenza infection in experimentally infected chickens and ducks. J Vet Diagn Invest. 2015 [Epub ahead of print].

485. Suarez DL, Das A, Ellis E. Review of rapid molecular diagnostic tools for avian influenza virus. Avian Dis. 2007;51(1 Suppl):201-8.

486. Capua I, Marangon S. The use of vaccination as an option for the control of avian influenza. Avian Pathol. 2003;32(4):335-43.

487. World Organization for Animal Health [OIE]. Manual of diagnostic tests and vaccines for terrestrial animals [online]. Paris; OIE; 2012. Avian influenza. Available at: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.03.04_AI.pdf. Accessed 16 Jun 2014.

488. United States Geological Survey [USGS]. National Wildlife Health Center. Wildlife health bulletin #05-03 [online]. USGS; 2005 Aug. Available at: http://www.nwhc.usgs.gov/publications/wildlife_health_bulletins/WHB_05_03.jsp. Accessed 25 Jan 2007.

489. ouma A, Chen H, Erasmus B, Jones P, Marangon S, Domenech J [OIE Ad Hoc Group on AI Vaccination Guidelines]. Vaccination: a tool for the control of avian influenza. Proceedings of a meeting. March 20-22, 2007. Verona, Italy. Dev Biol (Basel). 2007;130:3-167. Available at: http://www.oie.int/eng/info_ev/Other%20Files/A_Guidelines%20on%20AI%20vaccination.pdf. Accessed Dec 3 2010.

490. Villarreal C. Avian influenza in Mexico. Rev Sci Tech. 2009;28(1):261-5.

491. Chen H. Avian influenza vaccination: the experience in China. Rev Sci Tech. 2009;28(1):267-74.

492. Koch G, Steensels M, van den Berg T. Vaccination of birds other than chickens and turkeys against avian influenza. Rev Sci Tech. 2009;28(1):307-18.

493. Maas R, Tacken M, van ZD, Oei H. Dose response effects of avian influenza (H7N7) vaccination of chickens: serology, clinical protection and reduction of virus excretion. Vaccine. 2009;27(27):3592-7.

494. Swayne DE, Lee CW, Spackman E. Inactivated North American and European H5N2 avian influenza virus vaccines protect chickens from Asian H5N1 high pathogenicity avian influenza virus. Avian Pathol. 2006;35(2):141-6.

495. Bouma A, Claassen I, Natih K, Klinkenberg D, Donnelly CA, Koch G, van BM. Estimation of transmission parameters of H5N1 avian influenza virus in chickens. PLoS Pathog. 2009;5(1):e1000281.

496. van der Goot JA, Koch G, de Jong MC, van BM. Quantification of the effect of vaccination on transmission of avian influenza (H7N7) in chickens. Proc Natl Acad Sci U S A. 2005;102(50):18141-6.

497. Poetri ON, Bouma A, Murtini S, Claassen I, Koch G, Soejoedono RD, Stegeman JA, van BM. An inactivated H5N2 vaccine reduces transmission of highly pathogenic H5N1 avian influenza virus among native chickens. Vaccine. 2009;27(21):2864-9.

498. Bublot M, Pritchard N, Cruz JS, Mickle TR, Selleck P, Swayne DE. Efficacy of a fowlpox-vectored avian influenza H5 vaccine against Asian H5N1 highly pathogenic avian influenza virus challenge. Avian Dis. 2007;51(1 Suppl):498-500.

499. Rudolf M, Poppel M, Frohlich A, Breithaupt A, Teifke J, Blohm U, Mettenleiter T, Beer M, Harder T. Longitudinal 2 years field study of conventional vaccination against highly pathogenic avian influenza H5N1 in layer hens. Vaccine. 2010;28(42):6832-40.

500. Bos ME, Nielen M, Koch G, Stegeman A, de Jong MC. Effect of H7N1 vaccination on highly pathogenic avian influenza H7N7 virus transmission in turkeys. Vaccine. 2008;26(50):6322-8.

501. Capua I, Terregino C, Cattoli G, Toffan A. Increased resistance of vaccinated turkeys to experimental infection with an H7N3 low-pathogenicity avian influenza virus. Avian Pathol. 2004;33(2):158-63.

502. Karunakaran D, Newman JA, Halvorson DA, Abraham A. Evaluation of inactivated influenza vaccines in market turkeys. Avian Dis. 1987;31(3):498-503.

503. van der Goot JA, van BM, Stegeman A, van de Water SG, de Jong MC, Koch G. Transmission of highly pathogenic avian influenza H5N1 virus in Pekin ducks is significantly reduced by a genetically distant H5N2 vaccine. Virology. 2008;382(1):91-7.

504. Lee CW, Senne DA, Suarez DL. Effect of vaccine use in the evolution of Mexican lineage H5N2 avian influenza virus. J Virol. 2004;78(15):8372-81.

505. Jadhao SJ, Lee CW, Sylte M, Suarez DL. Comparative efficacy of North American and antigenically matched reverse genetics derived H5N9 DIVA marker vaccines against highly pathogenic Asian H5N1 avian influenza viruses in chickens. Vaccine. 2009;27(44):6247-60.

506. Eggert D, Thomas C, Spackman E, Pritchard N, Rojo F, Bublot M, Swayne DE. Characterization and efficacy determination of commercially available Central American H5N2 avian influenza vaccines for poultry. Vaccine. 2010;28(29):4609-15.

507. Capua I, Marangon S. Control of avian influenza in poultry. Emerg Infect Dis. 2006;12(9):1319-24.

508. Suarez DL. Overview of avian influenza DIVA test strategies. Biologicals. 2005;33(4):221-6.

509. Tian G, Zeng X, Li Y, Shi J, Chen H. Protective efficacy of the H5 inactivated vaccine against different highly pathogenic H5N1 avian influenza viruses isolated in China and Vietnam. Avian Dis. 2010;54(1 Suppl):287-9.

510. Promed Mail. PRO/AH> Avian influenza (46): Viet Nam, vaccine efficacy, RFI. Archive Number 20110527.1628. 2011. Available at http://www.promedmail.org. Accessed 5 Jan 2012.

511. Verhagen JH, Munster VJ, Majoor F, Lexmond P, Vuong O, Stumpel JB, Rimmelzwaan GF, Osterhaus AD, Schutten M, Slaterus R, Fouchier RA. Avian influenza A virus in wild birds in highly urbanized areas. PLoS One. 2012;7(6):e38256.

512. Kirunda H, Erima B, Tumushabe A, Kiconco J, Tugume T, Mulei S et al. Prevalence of influenza A viruses in livestock and free-living waterfowl in Uganda. BMC Vet Res. 2014;10:50.

513. De Marco MA, Foni E, Campitelli L, Delogu M, Raffini E, Chiapponi C, Barigazzi G, Cordioli P, Di TL, Donatelli I. Influenza virus circulation in wild aquatic birds in Italy during H5N2 and H7N1 poultry epidemic periods (1998 to 2000). Avian Pathol. 2005;34(6):480-5.

514. Harris MT, Brown JD, Goekjian VH, Luttrell MP, Poulson RL, Wilcox BR, Swayne DE, Stallknecht DE. Canada geese and the epidemiology of avian influenza viruses. J Wildl Dis. 2010;46(3):981-7.

515. Nallar R, Papp Z, Epp T, Leighton FA, Swafford SR, DeLiberto TJ, Dusek RJ, Ip HS, Hall J, Berhane Y, Gibbs SE, Soos C. Demographic and spatiotemporal patterns of avian influenza infection at the continental scale, and in relation to annual life cycle of a migratory host. PLoS One. 2015;10(6):e0130662.

516. Normile D, Enserink M. With change in the seasons, bird flu returns. Science. 2007;315:448.

517. Mathur MB, Patel RB, Gould M, Uyeki TM, Bhattacharya J, Xiao Y, Gillaspie Y, Chae C, Khazeni N. Seasonal patterns in human A (H5N1) virus infection: Analysis of global cases. PLoS One. 2014;9(9):e106171.

518. Chen H, Li Y, Li Z, Shi J, Shinya K, Deng G, Qi Q, Tian G, Fan S, Zhao H, Sun Y, Kawaoka Y. Properties and dissemination of H5N1 viruses isolated during an influenza outbreak in migratory waterfowl in western China. J Virol. 2006;80(12):5976-83.

519. Yuan Z, Zhu W, Chen Y, Zhou P, Cao Z, Xie J, Zhang C, Ke C, Qi W, Su S, Zhang G. Serological surveillance of H5 and H9 avian influenza A viral infections among pigs in southern China. Microb Pathog. 2013;64:39-42.

520. Marschall J, Schulz B, Harder Priv-Doz TC, Vahlenkamp Priv-Doz TW, Huebner J, Huisinga E, Hartmann K. Prevalence of influenza A H5N1 virus in cats from areas with occurrence of highly pathogenic avian influenza in birds. J Feline Med Surg. 2008;10(4):355-8.

521. Sun L, Zhou P, He S, Luo Y, Jia K, Fu C, Sun Y, He H, Tu L, Ning Z, Yuan Z, Wang H, Li S, Yuan L. Sparse serological evidence of H5N1 avian influenza virus infections in domestic cats, northeastern China. Microb Pathog. 2015;82:27-30.

522. Akerstedt J, Valheim M, Germundsson A, Moldal T, Lie KI, Falk M, Hungnes O. Pneumonia caused by influenza A H1N1 2009 virus in farmed American mink (*Neovison vison*). Vet Rec. 2012;170(14):362.

523. Yoon KJ, Schwartz K, Sun D, Zhang J, Hildebrandt H. Naturally occurring Influenza A virus subtype H1N2 infection in a Midwest United States mink (*Mustela vison*) ranch. J Vet Diagn Invest. 2012;24(2):388-91.

524. Gao HN, Lu HZ, Cao B, Du B, Shang H, Gan JH et al. Clinical findings in 111 cases of influenza A (H7N9) virus infection. N Engl J Med. 2013;368(24):2277-85.

525. Virlogeux V, Li M, Tsang TK, Feng L, Fang VJ, Jiang H, Wu P, Zheng J, Lau EH, Cao Y, Qin Y, Liao Q, Yu H, Cowling BJ. Estimating the distribution of the incubation periods of human avian influenza A(H7N9) virus infections. Am J Epidemiol. 2015;182(8):723-9.

526. Liem NT, Tung CV, Hien ND, Hien TT, Chau NQ, Long HT, Hien NT, Mai lQ, Taylor WR, Wertheim H, Farrar J, Khang DD, Horby P. Clinical features of human influenza A (H5N1) infection in Vietnam: 2004-2006. Clin Infect Dis. 2009;48(12):1639-46.

527. World Health Organization {WHO]. Avian influenza (“bird flu”) fact sheet [online]. WHO; 2006 Feb. Available at: http://www.who.int/mediacentre/factsheets/avian_influenza/en/index.html#humans.* Accessed 1 Aug 2007.

528. Brooks WA, Alamgir AS, Sultana R, Islam MS, Rahman M, Fry AM et al. Avian influenza virus A (H5N1), detected through routine surveillance, in child, Bangladesh. Emerg Infect Dis. 2009;15(8):1311-3.

529. Flu Trackers. H7N9 case list from Flu Trackers. 2014. Available at: http://www.flutrackers.com/forum/showpost.php?p=489904. Accessed 19 Jun 2014.

530. Ip DK, Liao Q, Wu P, Gao Z, Cao B, Feng L et al. Detection of mild to moderate influenza A/H7N9 infection by China's national sentinel surveillance system for influenza-like illness: case series. BMJ. 2013;346:f3693.

531. Hu Y, Lu S, Song Z, Wang W, Hao P, Li J et al. Association between adverse clinical outcome in human disease caused by novel influenza A H7N9 virus and sustained viral shedding and emergence of antiviral resistance. Lancet. 2013;381(9885):2273-9.

532. World Health Organization [WHO]. China–WHO joint mission on human infection with avian influenza A (H7N9) virus. 18–24 April 2013. Mission report. Geneva: WHO.. Available at: http://www.who.int/influenza/human.../influenza_h7n9/ChinaH7N9JointMissionReport2013.pdf. Accessed 2 May 2014.
533. Lv H, Han J, Zhang P, Lu Y, Wen D, Cai J, Liu S, Sun J, Yu Z, Zhang H, Gong Z, Chen E, Chen Z. Mild illness in avian influenza A(H7N9) virus-infected poultry worker, Huzhou, China, April 2013. Emerg Infect Dis. 2013;19(11):1885-8.
534. Kalthoff D, Bogs J, Harder T, Grund C, Pohlmann A, Beer M, Hoffmann B. Nucleic acid-based detection of influenza A virus subtypes H7 and N9 with a special emphasis on the avian H7N9 virus. Euro Surveill. 2014;19(10).
535. Hackett H, Bialasiewicz S, Jacob K, Bletchly C, Harrower B, Nimmo GR, Nissen MD, Sloots TP, Whiley DM. Screening for H7N9 influenza A by matrix gene-based real-time reverse-transcription PCR. J Virol Methods. 2014;195:123-5.
536. Marzoratti L, Iannella HA, Gomez VF, Figueroa SB. Recent advances in the diagnosis and treatment of influenza pneumonia. Curr Infect Dis Rep. 2012;14(3):275-83.
537. Kumar S, Henrickson KJ. Update on influenza diagnostics: lessons from the novel H1N1 influenza A pandemic. Clin Microbiol Rev. 2012;25(2):344-61.
538. Centers for Disease Control and Prevention [CDC]. Evaluation of rapid influenza diagnostic tests for influenza A (H3N2)v virus and updated case count--United States, 2012. MMWR Morb Mortal Wkly Rep. 2012;61(32):619-21.
539. Erlikh IV, Abraham S, Kondamudi VK. Management of influenza. Am Fam Physician. 2010;82(9):1087-95.
540. St George K. Diagnosis of influenza virus. Methods Mol Biol. 2012;865:53-69.
541.Centers for Disease Control and Prevention [CDC]. Seaonal influenza. Information for health care professionals [Website online]. CDC; 2014. Available at: http://www.cdc.gov/flu/professionals/index.htm. Accessed 16 Jun 2014
542. Klimov A, Balish A, Veguilla V, Sun H, Schiffer J, Lu X, Katz JM, Hancock K. Influenza virus titration, antigenic characterization, and serological methods for antibody detection. Methods Mol Biol. 2012;865:25-51.
543. Dong L, Bo H, Bai T, Gao R, Dong J, Zhang Y et al. A combination of serological assays to detect human antibodies to the avian influenza A H7N9 virus. PLoS One. 2014;9(4):e95612.
544. Kumar A. Pandemic H1N1 influenza. J Thorac Dis. 2011;3(4):262-70.
545. Dunning J, Baillie JK, Cao B, Hayden FG. Antiviral combinations for severe influenza. Lancet Infect Dis. 2014;14(12):1259-70.
546. Lamb S, McElroy T. Bronson alerts public to newly emerging canine flu. Florida Department of Agriculture and Consumer Services; 2005 Sept. Available at: http://doacs.state.fl.us/press/2005/09202005.html.* Accessed 27 Sept 2005.
547. National Institute of Allergy and Infectious Diseases 279, National Institutes of Health 279. Flu drugs [online]. NIAID, NIH; 2003 Feb. Available at: http://www.niaid.nih.gov/factsheets/fludrugs.htm.* Accessed 11 Nov 2006.
548. Public Health Agency of Canada. Pathogen Safety Data Sheet – Influenza virus (B and C). Pathogen Regulation Directorate, Public Health Agency of Canada; 2012 Apr. Available at: http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/influenza-grippe-b-c-eng.php. Accessed 16 June 2014.
549. Thorlund K, Awad T, Boivin G, Thabane L. Systematic review of influenza resistance to the neuraminidase inhibitors. BMC Infect Dis. 2011;11:134.
550. Yu H, Hua RH, Zhang Q, Liu TQ, Liu HL, Li GX, Tong GZ. Genetic evolution of swine influenza A (H3N2) viruses in China from 1970 to 2006. J Clin Microbiol. 2008;46(3):1067-75.
551. Kandun IN, Tresnaningsih E, Purba WH, Lee V, Samaan G, Harun S, Soni E, Septiawati C, Setiawati T, Sariwati E, Wandra T. Factors associated with case fatality of human H5N1 virus infections in Indonesia: a case series. Lancet. 2008;372(9640):744-9.
552. Smith NM, Bresee JS, Shay DK, Uyeki TM, Cox NJ, Strikas RA. Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb Mortal Wkly Rep. 2006;55(RR-10):1-42.
553. Govorkova EA, Baranovich T, Seiler P, Armstrong J, Burnham A, Guan Y, Peiris M, Webby RJ, Webster RG. Antiviral resistance among highly pathogenic influenza A (H5N1) viruses isolated worldwide in 2002-2012 shows need for continued monitoring. Antiviral Res. 2013;98(2):297-304.
554. Orozovic G, Orozovic K, Lennerstrand J, Olsen B. Detection of resistance mutations to antivirals oseltamivir and zanamivir in avian influenza A viruses isolated from wild birds. PLoS One. 2011;6(1):e16028.
555. Department of the Interior [DOI]. Appendix H: Employee health and safety guidance for avian influenza surveillance and control activities in wild bird populations [online]. DOI; 2007. Available at: http://www.doi.gov/emergency/pandemicflu/appendix-h.cfm. Accessed 16 Jun 2014.
556. Tumpey TM, Suarez DL, Perkins LE, Senne DA, Lee JG, Lee YJ, Mo IP, Sung HW, Swayne DE. Characterization of a highly pathogenic H5N1 avian influenza A virus isolated from duck meat. J Virol. 2002;76(12):6344-55.
557. Swayne DE, Beck JR. Experimental study to determine if low-pathogenicity and high-pathogenicity avian influenza viruses can be present in chicken breast and thigh meat following intranasal virus inoculation. Avian Dis. 2005;49(1):81-5.
558. Brown CC, Olander HJ, Senne DA. A pathogenesis study of highly pathogenic avian influenza virus H5N2 in chickens, using immunohistochemistry. J Comp Pathol. 1992;107(3):341-8.
559. Mo IP, Brugh M, Fletcher OJ, Rowland GN, Swayne DE. Comparative pathology of chickens experimentally inoculated with avian influenza viruses of low and high pathogenicity. Avian Dis. 1997;41(1):125-36.
560. Mase M, Eto M, Tanimura N, Imai K, Tsukamoto K, Horimoto T, Kawaoka Y, Yamaguchi S. Isolation of a genotypically unique H5N1 influenza virus from duck meat imported into Japan from China. Virology. 2005;339:101-9.
561. Hsu JL, Liu KE, Huang MH, Lee HJ. Consumer knowledge and risk perceptions of avian influenza. Poult Sci. 2008;87(8):1526-34.

562. United States Food and Drug Administration 296. FDA approves first U.S. vaccine for humans against the avian influenza virus H5N1. Press release P07-68. FDA; 2007 Apr. Available at: http://www.fda.gov/bbs/topics/NEWS/2007/NEW01611.html.* Accessed 31 Jul 2007.

563. Centers for Disease Control and Prevention [CDC]. Questions and answers. 2009 H1N1 flu (“swine flu”). CDC; 2009 Nov. Available at: http://www.cdc.gov/swineflu/.* Accessed 17 Nov 2009.

564. Arafa AS, Naguib MM, Luttermann C, Selim AA, Kilany WH, Hagag N et al. Emergence of a novel cluster of influenza A(H5N1) virus clade 2.2.1.2 with putative human health impact in Egypt, 2014/15. Euro Surveill. 2015;20(13):2-8.

565. Fiebig L, Soyka J, Buda S, Buchholz U, Dehnert M, Haas W. Avian influenza A(H5N1) in humans: new insights from a line list of World Health Organization confirmed cases, September 2006 to August 2010. Euro Surveill. 2011;16(32).

566. Le MT, Wertheim HF, Nguyen HD, Taylor W, Hoang PV, Vuong CD et al. Influenza A H5N1 clade 2.3.4 virus with a different antiviral susceptibility profile replaced clade 1 virus in humans in northern Vietnam. PLoS One. 2008;3(10):e3339.

567. Abdel-Ghafar AN, Chotpitayasunondh T, Gao Z, Hayden FG, Nguyen DH, de Jong MD, Naghdaliyev A, Peiris JS, Shindo N, Soeroso S, Uyeki TM. Update on avian influenza A (H5N1) virus infection in humans. N Engl J Med. 2008;358(3):261-73.

568. Peiris JS, Yu WC, Leung CW, Cheung CY, Ng WF, Nicholls JM, Ng TK, Chan KH, Lai ST, Lim WL, Yuen KY, Guan Y. Re-emergence of fatal human influenza A subtype H5N1 disease. Lancet. 2004;363(9409):617-9.

569. Oner AF, Dogan N, Gasimov V, Adisasmito W, Coker R, Chan PK, Lee N, Tsang O, Hanshaoworakul W, Zaman M, Bamgboye E, Swenson A, Toovey S, Dreyer NA. H5N1 avian influenza in children. Clin Infect Dis. 2012;55(1):26-32.

570. Kandeel A, Manoncourt S, Abd el KE, Mohamed Ahmed AN, El-Refaie S, Essmat H, Tjaden J, de Mattos CC, Earhart KC, Marfin AA, El-Sayed N. Zoonotic transmission of avian influenza virus (H5N1), Egypt, 2006-2009. Emerg Infect Dis. 2010;16(7):1101-7.

571. Wang TT, Parides MK, Palese P. Seroevidence for H5N1 influenza infections in humans: meta-analysis. Science. 2012;335(6075):1463.

572. Kwon D, Lee JY, Choi W, Choi JH, Chung YS, Lee NJ, Cheong HM, Katz JM, Oh HB, Cho H, Kang C. Avian influenza A (H5N1) virus antibodies in poultry cullers, South Korea, 2003-2004. Emerg Infect Dis. 2012;18(6):986-8.

573. Schultsz C, Nguyen VD, Hai lT, Do QH, Peiris JS, Lim W et al. Prevalence of antibodies against avian influenza A (H5N1) virus among cullers and poultry workers in Ho Chi Minh City, 2005. PLoS One. 2009;4(11):e7948.

574. Dung TC, Dinh PN, Nam VS, Tan LM, Hang NK, Thanh lT, Mai lQ. Seroprevalence survey of avian influenza A(H5N1) among live poultry market workers in northern Viet Nam, 2011. Western Pac Surveill Response J. 2014;5(4):21-6.

575. Le MQ, Horby P, Fox A, Nguyen HT, Le Nguyen HK, Hoang PM, Nguyen KC, de Jong MD, Jeeninga RE, Rogier van DH, Farrar J, Wertheim HF. Subclinical avian influenza A(H5N1) virus infection in human, Vietnam. Emerg Infect Dis. 2013;19(10):1674-7.

576. He F, Chen EF, Li FD, Wang XY, Wang XX, Lin JF. Human infection and environmental contamination with avian influenza A (H7N9) virus in Zhejiang Province, China: risk trend across the three waves of infection. BMC Public Health. 2015;15(1):931.

577. World Health Organization [WHO]. WHO risk assessment. Human infections with avian influenza A(H7N9) virus. WHO; 2014 Feb. Available at: http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/ Accessed 20 Jun 2014.

578. He L, Wu Q, Jiang K, Duan Z, Liu J, Xu H, Cui Z, Gu M, Wang X, Liu X, Liu X. Differences in transmissibility and pathogenicity of reassortants between H9N2 and 2009 pandemic H1N1 influenza A viruses from humans and swine. Arch Virol. 2014.

579. Fan M, Huang B, Wang A, Deng L, Wu D, Lu X et al. Human influenza A(H7N9) virus infection associated with poultry farm, northeastern China. Emerg Infect Dis. 2014;20(11):1902-5.

580. Arima Y, Vong S. Human infections with avian influenza A(H7N9) virus in China: preliminary assessments of the age and sex distribution. Western Pac Surveill Response J. 2013;4(2):1-3.

581. Feng L, Wu JT, Liu X, Yang P, Tsang TK, Jiang H et al. Clinical severity of human infections with avian influenza A(H7N9) virus, China, 2013/14. Euro Surveill. 2014;19(49).

582. Liu S, Sun J, Cai J, Miao Z, Lu M, Qin S, Wang X, Lv H, Yu Z, Amer S, Chai C. Epidemiological, clinical and viral characteristics of fatal cases of human avian influenza A (H7N9) virus in Zhejiang Province, China. J Infect. 2013;67(6):595-605.

583. Guo L, Zhang X, Ren L, Yu X, Chen L, Zhou H et al. Human antibody responses to avian influenza A(H7N9) virus, 2013. Emerg Infect Dis. 2014;20(2):192-200.

584. Xu W, Lu L, Shen B, Li J, Xu J, Jiang S. Serological investigation of subclinical influenza A(H7H9) infection among healthcare and non-healthcare workers in Zhejiang Province, China. Clin Infect Dis. 2013;57(6):919-21.

585. Wang W, Peng H, Zhao P, Qi Z, Zhao X, Wang Y, Wang C, Hang X, Ke J. Cross-reactive antibody responses to the novel avian influenza A H7N9 virus in Shanghai adults. J Infect. 2014.

586. Yang S, Chen Y, Cui D, Yao H, Lou J, Huo Z et al. Avian-origin influenza A(H7N9) infection in influenza A(H7N9)-affected areas of China: a serological study. J Infect Dis. 2014;209(2):265-9.

587. Wang X, Fang S, Lu X, Xu C, Cowling BJ, Tang X et al. Seroprevalence to avian influenza A(H7N9) virus among poultry workers and the general population in southern China: A Longitudinal Study. Clin Infect Dis. 2014;59(6):e76-e83.

588. Chen J, Ma J, White SK, Cao Z, Zhen Y, He S, Zhu W, Ke C, Zhang Y, Su S, Zhang G. Live poultry market workers are susceptible to both avian and swine influenza viruses, Guangdong Province, China. Vet Microbiol. 2015 [Epub ahead of print].

589. Zhou P, Zhu W, Gu H, Fu X, Wang L, Zheng Y, He S, Ke C, Wang H, Yuan Z, Ning Z, Qi W, Li S, Zhang G. Avian influenza H9N2 seroprevalence among swine farm residents in China. J Med Virol. 2014;86(4):597-600.

590. Ahad A, Thornton RN, Rabbani M, Yaqub T, Younus M, Muhammad K, Mahmood A, Shabbir MZ, Kashem MA, Islam MZ, Mangtani P, Burgess GW, Tun HM, Hoque MA. Risk factors for H7 and H9 infection in commercial poultry farm workers in provinces within Pakistan. Prev Vet Med. 2014;117(3-4):610-4.
591. Khan SU, Anderson BD, Heil GL, Liang S, Gray GC. A systematic review and meta-analysis of the seroprevalence of influenza A(H9N2) infection among humans. J Infect Dis. 2015;212(4):562-9.
592. Khurelbaatar N, Krueger WS, Heil GL, Darmaa B, Ulziimaa D, Tserennorov D, Baterdene A, Anderson BD, Gray GC. Sparse evidence for equine or avian influenza virus infections among Mongolian adults with animal exposures. Influenza Other Respi Viruses. 2013;7(6):1246-50.
593. Puzelli S, Di Trani L., Fabiani C, Campitelli L, De Marco MA, Capua I, Aguilera JF, Zambon M, Donatelli I. Serological analysis of serum samples from humans exposed to avian H7 influenza viruses in Italy between 1999 and 2003. J Infect Dis. 2005;192(8):1318-22.
594. Shafir SC, Fuller T, Smith TB, Rimoin AW. A national study of individuals who handle migratory birds for evidence of avian and swine-origin influenza virus infections. J Clin Virol. 2012;54(4):364-7.
595. Qi W, Su S, Xiao C, Zhou P, Li H, Ke C, Gray GC, Zhang G, Liao M. Antibodies against H10N8 avian influenza virus among animal workers in Guangdong Province before November 30, 2013, when the first human H10N8 case was recognized. BMC Med. 2014;12:205.
596.Canadian Food Inspection Agency[CFIA]. H1N1 flu virus - advice for veterinarians and swine producers. CFIA; Aug 2012. Available at: http://www.inspection.gc.ca/animals/terrestrial-animals/diseases/other-diseases/h1n1-flu-virus/advice/eng/1344123804133/1344123976857. Accessed 17 June 2012.
597. Juozapaitis M, Aguiar ME, Mena I, Giese S, Riegger D, Pohlmann A, Hoper D, Zimmer G, Beer M, Garcia-Sastre A, Schwemmle M. An infectious bat-derived chimeric influenza virus harbouring the entry machinery of an influenza A virus. Nat Commun. 2014;5:4448.
598. Bae YJ, Lee SB, Min KC, Mo JS, Jeon EO, Koo BS, Kwon HI, Choi YK, Kim JJ, Kim JN, Mo IP. Pathological evaluation of natural cases of a highly pathogenic avian influenza virus, subtype H5N8, in broiler breeders and commercial layers in South Korea. Avian Dis. 2015;59(1):175-82.

* Link defunct as of 2015

