Avian Influenza

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Etiology

Avian influenza results from infection by viruses belonging to the species *influenza A virus*, genus *influenzavirus A* and family Orthomyxoviridae. Influenza A viruses are classified into subtypes based on two surface proteins, the hemagglutinin (HA) and neuraminidase (NA). 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. The viral HA, and to a lesser extent the NA, are major targets for the immune response. There is ordinarily little or no cross-protection between different HA or NA types.

Influenza viruses in birds are classified as either low pathogenic (also called low pathogenicity) 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 associated with HPAI viruses. To date, the fully virulent HPAI viruses found in nature have always contained H5 or H7, although there are rare examples of other viruses that could technically be considered HPAI.

Species Affected

The vast majority of LPAI viruses are maintained in asymptomatic wild birds in aquatic habitats. These birds are thought to be their natural reservoir 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). Some aquatic species in other orders might also be maintenance hosts. LPAI viruses seem to be uncommon in most wild birds that live on land (terrestrial birds). However, these birds can also become infected if they are exposed. HPAI viruses are not normally found in wild birds, although a few subtypes have been detected, and some have caused outbreaks.

Domesticated birds can be infected by avian influenza viruses, although susceptibility appears to differ between species. Poultry are readily infected by both LPAI and HPAI viruses. When LPAI viruses from wild birds are transferred to poultry, they 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. Viruses that have adapted to poultry rarely become re-established in wild birds, although they may infect them transiently. Many different viruses can cause disease in chickens and turkeys, but three viral lineages are currently of particular concern

Asian lineage H5N1 avian influenza viruses

The A/goose/Guangdong/1996 lineage ('Asian lineage') of H5N1 HPAI viruses seems to have a particularly wide host range. In addition to domesticated birds, these viruses have been found in a large number of wild or captive avian species. Whether wild birds can maintain these viruses for long periods (or indefinitely), or are repeatedly infected from poultry, is still controversial. Asian lineage H5N1 HPAI viruses can also infect many species of mammals, and their full host range is probably not yet known. To date, they have been found in pigs, housecats, several species of large felids in zoos, dogs, donkeys, stone martens (*Mustela foina*), raccoon dogs (*Nyctereutes procyonoides*), palm civets (*Chrotogale owstoni*), plateau pikas (*Ochotona curzoniae*) and a wild mink (*Mustela vison*). Serological evidence of infection or exposure has been reported in horses and raccoons. Experimental infections have been established in cats, dogs, foxes, pigs, ferrets, laboratory rodents, cynomolgus macaques (*Macaca fascicularis*) and rabbits. Cattle could be experimentally infected with viruses isolated from

cats, but serological studies in Egypt suggest that cattle, buffalo, sheep and goats are not normally infected. Reassortants that contain gene segments from H5N1 viruses (e.g., H5N2, H5N5 and H5N8 HPAI viruses) have also been found among poultry, and some of these viruses can cause illness in mammals.

Geographic Distribution

LPAI viruses are cosmopolitan in wild birds. Different viral lineages circulate in North America and Eurasia, although reassortment occurs between these lineages at some locations. LPAI viruses are usually absent from commercial poultry in developed nations, but they may be present in other domesticated birds. The H9N2 viruses circulating in poultry are currently limited to Eurasia. The zoonotic H7N9 LPAI viruses causing outbreaks in mainland China have not been reported from other regions, except as imported cases in travelers.

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 Asian or Middle Eastern countries, with outbreaks occurring at times in other parts of the Eastern Hemisphere

Transmission

In birds, avian influenza viruses are shed in the feces and respiratory secretions. Fecal-oral transmission is the predominant means of spread in aquatic wild bird reservoirs. Respiratory transmission is thought to be unimportant in most wild birds, but it can occur with a few viruses or in some hosts, particularly those that live on land. Asian lineage H5N1 HPAI viruses, for instance, can be shed mainly in the respiratory secretions even from wild waterfowl. 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. Most chickens usually excrete LPAI viruses for a week, and a minority of the flock for up to two weeks, but some species of birds, including waterfowl, may shed some LPAI or HPAI viruses for a few weeks. HPAI viruses have also been found in the yolk and albumen of eggs from chickens, turkeys and quail. LPAI virus shedding in eggs is either nonexistent or very rare. Fomites can be important in transmission, and flies may act as mechanical vectors. One recent study suggested that, under certain conditions, airborne spread might be possible between farms.

People and other mammals are usually infected with avian influenza viruses during close contact with birds or their tissues, although indirect contact via fomites or other means is also thought to be possible. Most viruses are probably acquired via the respiratory tract, but the eye may also act as an entry point. A few Asian lineage H5N1 HPAI virus infections in animals, and rare cases in humans, were likely acquired by eating raw tissues from infected birds. Housecats in an animal shelter might have become infected by ingesting fecal matter from a sick swan, during grooming. Infected animals and people shed avian influenza viruses mainly in respiratory secretions. Fecal shedding has been reported occasionally, but its significance is still uncertain. Asian lineage H5N1 HPAI viruses were also detected in the urine of some mammals. Transplacental transmission may be possible with certain viruses (e.g., Asian lineage H5N1 HPAI viruses) that can spread beyond the respiratory tract.
Influenza A viruses that infect species other than their usual hosts tend to be transmitted inefficiently, and do not typically continue to circulate in that population. However, on rare occasions in the past, a virus has continued to circulate in the new host, either “whole” or after reassorting with another influenza virus. Limited host-to-host transmission has been reported between mammals infected with some avian influenza viruses, including Asian lineage H5N1 HPAI viruses. These viruses were transmitted between zoo tigers in one outbreak, and experimentally between sick cats; however, there was no evidence of transmission from asymptomatic, naturally infected cats. Pigs might transmit this virus to a limited extent within an infected herd. Person-to-person transmission of these H5N1 viruses seems to be rare, and appears to require close, unprotected contact. Likewise, a few family clusters suggest that the Chinese H7N9 LPAI virus might be transmitted between humans during close

contact, but common source exposure is hard to rule out, and most infected people did not seem to transmit this virus to others.

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 theflock. 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.

Clinical Signs

Low pathogenic avian influenza

LPAI viruses usually cause subclinical infections or mild illnesses in poultry and other birds. Decreased egg production and quality, 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. Illnesses exacerbated by factors such as concurrent infections or young age can be more severe. Some gallinaceous game birds (e.g., pheasants, quail) infected with LPAI viruses have been asymptomatic, while others had clinical signs including lethargy, respiratory signs, conjunctivitis, decreased egg production and/or diarrhea. One study reported neurological signs and elevated mortality in guinea fowl infected with an H7N1 virus. Some Eurasian H9N2 viruses appear to be more virulent than most LPAI viruses in chickens and quail.
High mortality has been seen in young ostriches during some LPAI outbreaks; however, one outbreak virus caused only green diarrhea in experimentally infected young birds. Domesticated waterfowl are often infected subclinically, although there may be mild signs such as sinusitis. Wild birds infected with LPAI viruses usually have few or no obvious clinical signs, although subtle physiological or behavioral effects have been described.

HPAI viruses in birds

HPAI viruses usually cause severe illness in chickens and turkeys, and few birds in infected flocks survive. Decreased feed and water intake, with other nonspecific systemic, respiratory and/ or neurological signs (e.g., depression, edema and cyanosis of the unfeathered skin, diarrhea, ecchymoses on the shanks and feet, coughing) are common, but no signs are pathognomonic, and sudden death can also be seen. In rare cases, an H5 or H7 virus causes only mild illness in chickens and turkeys, although it has a genetic signature that classifies it as an HPAI virus. Such viruses may have been isolated when they were evolving to become more virulent.
HPAI virus infections may be asymptomatic, mild or severe in other birds, including gallinaceous birds other than chickens and turkeys. Anorexia, lethargy, neurological signs, diarrhea and sudden death have been reported in some gallinaceous game birds, but milder or minimal signs were reported in some flocks. Domesticated waterfowl tend to be mildly affected, but respiratory signs (e.g., sinusitis), diarrhea, 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. Pigeons are also thought to be relatively resistant to disease, although there have been reports of sporadic deaths and rare outbreaks. Young ostriches less than 6 months of age are usually much more severely affected than adults, and can have nonspecific signs, dyspnea; green urine, diarrhea or hemorrhagic diarrhea, with increased mortality. Some evidence suggests that HPAI viruses might not be more virulent than LPAI viruses in this species.
Wild birds or captive wild species can be affected by some HPAI viruses, although susceptibility to infection and the occurrence of clinical signs can differ between species. The clinical signs caused by Asian lineage H5N1 HPAI viruses ranged from nonspecific signs alone (sometimes with high mortality) to diarrhea, respiratory distress and/or neurological signs.

Post Mortem Lesions

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. 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. A small number of birds may have signs of acute renal failure and visceral urate deposition.

Highly pathogenic avian influenza in birds

The lesions in chickens and turkeys are highly variable and resemble those found in other systemic avian diseases. 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. 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). However, the gross lesions in some outbreaks may not fit the classical pattern, and birds that die peracutely may have few or no lesions.

The reported lesions in other gallinaceous birds include necrotic lesions in the pancreas, splenomegaly with parenchymal mottling, renal lesions, hemorrhages in internal organs and skeletal muscles, and pulmonary lesions. However, some lesions seen in chickens and turkeys, such as cyanosis and hemorrhagic lesions in unfeathered skin, may not be as prominent. Gross lesions of hepatitis and peritonitis, with other secondary lesions, have been seen in ostriches infected with avian influenza viruses. Petechial hemorrhages, pancreatic lesions, pulmonary congestion and edema, and other lesions have been reported in other species of birds infected with HPAI viruses.