Canine Influenza

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Importance

Influenza is a viral disease that has long been known to affect birds and some mammals, but was only recently recognized in dogs. Each influenza virus is maintained in one or more related host species; however, host specificity is not absolute. A virus may occasionally infect other animals, or on rare occasions, become adapted to a new species. No influenza viruses were known to circulate in dogs until 2004-2006, when a virus caused outbreaks of severe and often fatal respiratory disease among racing greyhounds in the U.S. This virus was acquired from horses, and probably entered greyhound populations several years before these outbreaks. Although it has spread to other dogs since this time, the illness in these animals has been more typical of influenza. The most common syndrome is a relatively mild upper respiratory disease with a persistent cough. Pneumonia is possible, generally as the result of secondary infection with bacteria or mycoplasma, but uncommon. At present, infections tend to be seen mainly in animal shelters, kennels, dog day care facilities, or other sites where groups of susceptible dogs are in close contact. This virus does not seem to have spread widely in other pets, and it has not yet been reported outside North America.

A second canine influenza virus was recognized in 2007, when a different virus caused an outbreak of severe respiratory disease in South Korea. This virus seems to have been acquired from birds, and may have entered canine populations around 2005. It has since been reported in China and Thailand, and can affect cats as well as dogs. Most reported clinical cases have been severe, but antibodies have been found in significant numbers of healthy dogs and cats, suggesting that some animals have milder illnesses.

Other influenza viruses can also affect dogs, without persisting in canine populations. Equine influenza viruses have caused a few small outbreaks, and there are reports of clinical cases caused by viruses adapted to birds or humans.

Etiology

Canine influenza viruses belong to the species *influenza A virus*, genus *Influenzavirus A*, and family Orthomyxoviridae. Other influenza A viruses infect birds (avian influenza viruses), horses and other equids (equine influenza viruses), pigs (swine influenza viruses) or people (human influenza A viruses). Influenza A viruses are classified into subtypes based on two surface proteins, the hemagglutinin (HA) and neuraminidase (NA). The subtype designation consists of the HA and NA found in that virus (e.g., H1N2). While at least 16 types of hemagglutinins (H1 to H16), and 9 neuraminidases (N1 to N9) are known to exist in birds, and two additional HA and NA types occur in bats, only a few avian subtypes and no bat subtypes have adapted to circulate in other mammals.

Influenza A viruses are extremely variable, and two viruses that share a subtype may be only distantly related. Nevertheless, all influenza A viruses are similar enough that they can 'reassort,' exchanging gene segments to produce progeny containing elements of both parental viruses – regardless of their original host specificity or subtype. Influenza A viruses can also infect species other than the host to which they are adapted, and on rare occasions, they may adapt to circulate in a new host. [The 'Influenza' factsheet contains a more extensive description of these processes.] Dogs have acquired two influenza viruses since 1999, an H3N8 virus that came from horses, and an H3N2 virus that came from birds. The North American H3N8 canine influenza virus seems to have jumped directly from horses to dogs, probably in the late 1990s or early 2000s. It is most closely related to the 'Florida lineage' of H3N8 equine influenza viruses, which emerged in the early 1990s. The H3N8 canine influenza virus is maintained in dog populations, and has diverged considerably from equine influenza viruses. It no longer seems to be capable of replicating efficiently in horses. The H3N2 canine influenza virus found in Asia seems to have originated in birds. It is reported to contain gene segments that may have come from several different avian influenza viruses. Based on evidence of experimental dog-to-dog transmission, and serological evidence from parts of Asia, this virus also appears to

be circulating among dogs. One study indicated that it may have infected dogs in South Korea since 2005.

Other influenza A viruses are also found sporadically in dogs, but are not maintained in canine populations, and are not considered to be canine influenza viruses. They include H3N8 equine influenza viruses, which have caused a few outbreaks in dogs exposed to infected horses, and human influenza viruses including the 2009 pandemic H1N1 influenza virus. An H3N1 virus, which seems to be the result of reassortment between the H3N2 canine influenza virus and the 2009 pandemic H1N1 virus, was recently isolated from a dog with respiratory signs in Korea. Dogs have also been affected by some viruses found in poultry, such as the Asian lineage H5N1 highly pathogenic avian influenza (HPAI) viruses, an H5N2 HPAI virus that is closely related to this virus, and H9N2 viruses. They might be susceptible to some viruses from wild birds.

Species Affected

As of 2014, the H3N8 canine influenza virus has only been reported in dogs. Its ability to replicate in horses appears to be greatly reduced, with low or absent virus shedding, and inefficient transmission from experimentally infected horses to naive horses. One study reported that horses were not infected when kept in close contact with experimentally infected dogs. In laboratory studies, the H3N8 canine influenza virus was not transmitted readily to chickens, turkeys or ducks.

The H3N2 canine influenza virus has caused clinical cases in dogs and cats, and antibodies to this virus have been found in both species. Dogs and cats can be infected by contact with experimentally infected dogs, and experimentally infected cats can transmit the virus to other cats. Ferrets can become infected after direct inoculation of the virus in the laboratory, but they seem to be less susceptible: ferrets did not become infected after exposure to experimentally infected dogs, and ferret-to-ferret transmission was limited. Attempts to transmit the H3N2 canine influenza virus to chickens and ducks were unsuccessful.

Geographic Distribution

The H3N8 canine influenza virus has been detected, at least sporadically, in most states in the U.S. The distribution of this virus is patchy; in some cases, it caused an outbreak or was detected serologically in an area, but later disappeared. There is no evidence that it currently circulates outside the U.S. As of 2014, the H3N2 canine influenza virus has only been reported in Korea, China and Thailand. A serological study found no evidence of its presence in Japan.

Infections with viruses not adapted to dogs have been reported in various regions where the virus is endemic. Human influenza viruses occur worldwide, and H3N8 equine influenza viruses are widely distributed. The avian influenza viruses that have affected dogs are currently found only in the Eastern Hemisphere (most often in Asia and the Middle East), but dogs may also be susceptible to viruses that occur in other locations.

Transmission

In mammals, influenza viruses are usually transmitted in droplets and aerosols created by coughing and sneezing, and by contact with nasal discharges, either directly or on fomites. Close contact and closed environments favor transmission. The H3N8 and H3N2 canine influenza viruses are both found in respiratory secretions, as is typical of mammalian influenza viruses. Fecal shedding has not been reported for either virus.

The H3N8 canine influenza virus can be detected in the respiratory secretions of both symptomatic and subclinically infected dogs. Dogs can shed this virus for as long as 7 days, based on the detection of infectious virus, although viral RNA may be found up to 10 days by PCR, Virus shedding peaks before the onset of severe clinical signs, and the highest titers occurred 3-4 days after inoculation in experimentally infected puppies. Overall, virus titers seem to be low, and the H3N8 canine influenza virus does not appear to spread rapidly in the community. However, transmission can occur more efficiently where groups of susceptible dogs are in close contact (e.g., in a kennel).

The H3N2 canine influenza virus might be transmitted more efficiently. Experimentally infected dogs shed this virus in nasal secretions from one to 8 days after inoculation, with peak virus excretion occurring early in this period. However, some animals still had evidence of infection in the lungs and nasal tissues at 14 days. Treatment with glucocorticoids (prednisolone) was reported to prolong virus shedding; in one experiment, the H3N2 canine influenza virus could be detected in the nasal secretions of some treated dogs for as long as 13 days, compared to 8 days in the controls. Experimentally infected cats shed this virus for up to 7 days.

Dogs infected with other viruses (not adapted to dogs) may or may not transmit them to others in close contact. There seems to be no significant dog-to-dog transmission of H3N8 equine influenza viruses.

There is no specific information on the persistence of canine influenza viruses in the environment; however, it is likely to be similar to other mammalian influenza viruses. Human influenza A viruses seem to remain viable for less than 24-48 hours on most surfaces, with recovery from porous surfaces sometimes lasting less than 8-12 hours. Nevertheless, some data indicate that they might survive longer on some fomites or in some conditions. Low temperatures and protection from sunlight enhance virus survival. Swine influenza viruses and avian influenza viruses can persist in feces for <1 day to 2 weeks or longer, depending on environmental factors including desiccation. Avian influenza viruses and human influenza A viruses may be found for weeks or months in some types of water

(e.g., distilled), although they might be inactivated faster in aquatic environments that contain normal microbial flora.

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. Common household agents including 1% bleach, 10% malt vinegar or 0.01-0.1% dishwashing liquid (washing up liquid), as well as antimicrobial wipes, were found to destroy the viability of human influenza viruses, although hot water (55°C; 131°F) did not eliminate these viruses rapidly. 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).

Incubation Period

The incubation period for H3N8 canine influenza is thought to be one to 5 days, with most cases appearing in 2 to 3 days.

Fever has been reported as soon as one to 3 days in dogs inoculated with the H3N2 canine influenza virus, with respiratory signs developing at 2 to 8 days. In experimentally infected cats, clinical signs first appeared after 2 to 7 days.

Clinical Signs

Canine influenza (H3N8)

The most common presentation in H3N8 canine influenza is a mild illness that resembles infectious tracheobronchitis (kennel cough) or other upper respiratory diseases. An initial (usually low grade) fever may be followed by a persistent cough, which tends to be nonproductive and dry (in cases not complicated by co-infections), but may also be soft and moist. The cough can last for up to 3 weeks regardless of treatment. Other common clinical signs include nasal discharge, sneezing, ocular discharge, lethargy and anorexia. The nasal discharge can start clear but may quickly become mucopurulent. Purulent discharges seem to resolve with antibiotics, suggesting the involvement of secondary bacterial infections. Some dogs have only a low fever, without respiratory signs, and asymptomatic seroconversion has been reported.

More severely affected dogs exhibit a high fever with an increased respiratory rate and other signs of pneumonia or bronchopneumonia. Severe lung involvement seems to occur mainly in cases with secondary bacterial or mycoplasmal infections. During the initial outbreaks among racing greyhounds, some dogs were found dead peracutely with evidence of hemorrhages in the respiratory tract. This syndrome does not seem to be prominent in pets.

Experimentally infected horses had mild clinical signs compared to horses inoculated with equine influenza viruses, or remained asymptomatic.

Canine influenza (H3N2)

Clinical cases reported in dogs have been characterized by fever (which may be low) and respiratory signs including nasal discharge, sneezing, coughing and anorexia. The nasal discharge was described as copious in one report. Dogs affected in early reports from South Korea and China were severely ill, and although few cases were reported, a number of them were fatal. Similar signs were described during a recent outbreak at a veterinary hospital in Thailand. The severity of the clinical signs was not described in this report, but no deaths are mentioned. Some of these dogs were ill for as long as 7-10 days. Experimentally infected dogs also developed respiratory signs (fever, sneezing, coughing, nasal discharges and abdominal breathing). However, antibodies to the H3N2 canine influenza virus have been reported in dogs without a history of severe respiratory disease, suggesting that milder illnesses or subclinical infections are also possible.

The H3N2 canine influenza virus also seems to cause illness in cats. This virus was isolated from a cat that died during an outbreak of severe respiratory disease among dogs and cats at an animal shelter. The clinical signs in the cats included dyspnea, tachypnea and lethargy. Co-infections might have played some role in this outbreak, as *Bordetella bronchiseptica* was also found in at least one cat. Cats that were experimentally infected with the H3N2 canine influenza virus had elevated temperatures, lethargy and respiratory signs including coughing, sneezing, ocular and nasal discharge, conjunctivitis and abdominal breathing. Antibodies to the H3N2 canine influenza virus have also been reported in apparently healthy cats.

Although ferrets were not very susceptible to this virus, some experimentally infected animals developed clinical signs. Sneezing was seen most often, and some animals were lethargic and anorectic.

Other influenza viruses in dogs

In the U.K., an H3N8 equine influenza virus caused a limited outbreak among foxhounds in 2002. The disease was characterized by coughing, lethargy and weakness, sometimes progressing to loss of consciousness, and was diagnosed as bronchointerstitial pneumonia. One dog died and several were euthanized. Clinical signs in dogs infected with H3N8 equine influenza viruses in Australia included anorexia, depression, slight nasal discharge, and in some cases, a cough that persisted for several weeks. All of these dogs recovered. Dogs that were experimentally infected with H3N8 equine influenza viruses remained asymptomatic or had very mild clinical signs (e.g., periodic anorexia and sneezing).

The 2009 pandemic H1N1 virus was isolated from 2 dogs in China, one with a severe cough and mild depression

and anorexia, and the other with severe cough, nasal discharge, fever, enlarged mandibular lymph nodes and radiological evidence of pneumonia. This virus was also isolated from a dog in the U.S. with clinical signs of lethargy, anorexia, fever and coughing, and radiological evidence of pneumonia. All three animals recovered with treatment, which included hospitalization and antibiotics in the two severe cases. Mild fever, occasional mild coughing, and nasal discharge were the only clinical signs in experimentally infected dogs. An H3N1 virus, which appears to be a reassortant between the canine H3N2 virus and the human 2009 pandemic H1N1 virus, was isolated from a dog with respiratory signs in Korea. Dogs inoculated with this virus remained asymptomatic and had only mild lung lesions.

A few infections caused by avian influenza viruses have also been described. One dog that ate poultry infected with an Asian lineage H5N1 HPAI virus developed a high fever, with panting and lethargy, and died the following day. However, antibodies to H5N1 viruses, together with virological evidence of infection, were also found in some stray dogs during avian influenza virus surveillance in China. Clinical signs in experimentally infected dogs ranged from transient fever, conjunctivitis or no signs, to fever, anorexia, diarrhea, conjunctivitis, and severe respiratory signs. The most severe illnesses occurred in dogs that had been inoculated by a route that bypasses some normal respiratory defenses (intratracheal inoculation). Dogs inoculated via the nose had milder signs. One H5N2 HPAI virus was isolated from a dog with respiratory signs in China, and 5 other dogs were seropositive. Dogs inoculated with this virus developed mild respiratory signs (conjunctivitis, sneezing, nasal discharge, mild coughing). Dogs that were experimentally infected with H9N2 viruses from poultry had respiratory signs, and evidence of infection was reported in both healthy and sick dogs in China. Dogs inoculated with an H6N1 avian influenza virus from waterfowl had no clinical signs other than a transient fever.

Post Mortem Lesions

Canine influenza (H3N8)

Fatal H3N8 canine influenza cases in racing greyhounds were often characterized by hemorrhages in the lungs, mediastinum and pleural cavity. The lungs also exhibited signs of severe pneumonia, and were dark red to black. Fibrinous pleuritis was seen in some cases. In other dogs, fatal cases seem to be characterized mainly by suppurative secondary bacterial pneumonia, and hemorrhagic pneumonia does not appear to be common. Bronchitis and tracheitis were the only significant lesions in 5 shelter dogs that were euthanized primarily for a chronic cough unresponsive to antibiotics.

Based on studies in experimentally infected dogs, the early lesions are thought to be tracheitis and bronchitis, with some extension to the bronchioles. Variable lower respiratory tract lesions may be seen, especially later in the illness, and may include petechiae, areas of consolidation and other lesions consistent with viral pneumonia.

Canine influenza (H3N2)

Severe hemorrhagic, cranioventral bronchointerstitial pneumonia was reported in most fatal cases of canine H3N2 influenza in naturally infected dogs; however, only partial necropsies were available and only for a limited number of cases. Experimentally infected dogs also had signs of pneumonia with multifocal to coalescing reddish consolidation, edema and hemorrhages in the lungs. No lesions were found outside the respiratory tract.

During an outbreak of severe respiratory disease in cats, the lesions included severe bronchopneumonia with consolidation in large areas of the lung, and pulmonary edema in some cats. Some cats were coinfected with other respiratory pathogens.

Diagnostic Tests

Canine influenza (H3N8)

Serology and reverse transcription polymerase chain reaction (RT-PCR) assays are the most reliable methods for detecting H3N8 canine influenza. Hemagglutination inhibition is considered the serological test of choice. Virus neutralization (microneutralization test) can also be done, but this test is usually too cumbersome for routine use. Antibodies usually develop 7-10 days after infection and continue to rise to high levels around 14 days. Although acute and convalescent titers are ideal, most dogs are not expected to have pre-existing titers to this virus, and a single sample collected more than 7 days after the onset of clinical signs can be very useful.

RT-PCR is the most reliable method to detect the virus directly, due to its sensitivity. Nasal swabs are the preferred sample from live dogs, and were more likely to yield virus than nasopharyngeal swabs in experimentally infected dogs. Lung tissue samples are collected at necropsy. Virus isolation may also be done, but it is unlikely to be successful in a dog that has had clinical signs for more than 3 days. The H3N8 canine influenza virus has been isolated in both embryonated eggs and cell cultures (MDCK cells); some viruses have been recovered in only eggs or cells, while others can be isolated in both systems. Both virus isolation and RT-PCR can fail to detect the virus in infected dogs if the samples are collected too late.

Antigen-capture ELISA tests do not seem to be reliable in individual dogs, probably because virus shedding is low, and the timing of sample collection is not always optimal. A recent study suggested that the sensitivity of these tests is much lower than RT-PCR and lower than virus isolation, and false positives were also common. However, they may be useful during investigations of outbreaks at kennels or other facilities housing groups of dogs.

Canine influenza (H3N2)

Little has been published about diagnostic testing for H3N2 canine influenza, but virus isolation and RT-PCR were used in some outbreaks. Nasal swabs were collected from some live dogs. An ELISA test that detects antibodies to the viral nucleoprotein has also been used in South Korea. Serological tests may be helpful.

Treatment

Treatment is supportive, and often includes antibiotics to control secondary bacterial infections. Although antiviral drugs (e.g., neuraminidase inhibitors) are sometimes used in cases of human influenza, these drugs have not been tested in canine influenza. They are most useful during the first 48 hours after the onset of clinical signs, and in many cases, this period is likely to have passed by the time the dog is seen by a veterinarian. The risk that viruses might become resistant to these drugs is also a concern.

Control

Disease reporting

Official reporting requirements for canine influenza differ between areas, and this disease is currently reportable in some U.S. states, but not others. However, information about outbreaks is often disseminated even in locations with no formal requirement to report this disease.

Prevention

Vaccines for canine influenza are available in some areas. A licensed vaccine for the H3N8 canine influenza virus is commercially available in the U.S. An H3N2 canine influenza virus has also been approved in South Korea.

Influenza viruses usually spread most readily when susceptible animals are in close contact. Infection control measures are similar to those used for other contagious respiratory diseases, and include isolation of infected animals; cleaning and disinfection of cages, bowls and other fomites; and hygiene measures including hand washing. Clothing can be cleaned by washing it with detergent at normal laundry temperatures.

Veterinarians should be alert to announcements of canine influenza outbreaks in an area. Clients should also be advised to consult a veterinarian if their dog develops signs of a respiratory illness, and should be questioned about potential exposures to other dogs (e.g., recent boarding). When outbreaks occur at establishments, quarantines and the isolation of infected animals can reduce virus dissemination to the community and within the facility.

Morbidity and Mortality

In mammals, the severity of influenza can differ with the virus, and is also influenced by host factors such as immunity, age and concurrent diseases. Uncomplicated infections with influenza viruses adapted to that host tend to be associated with high morbidity rates, low mortality rates and rapid recovery. More severe disease and higher mortality rates may be seen in young, old or debilitated animals. Secondary bacterial infections can exacerbate the clinical signs, prolong recovery and result in complications such as pneumonia. Infections with viruses not adapted to that host vary widely in severity; some viruses typically cause asymptomatic infections and mild illnesses, while others tend to cause severe disease.

Canine influenza (H3N8)

Although H3N8 canine influenza was first reported in racing greyhounds, all breeds are now considered to be susceptible. The greatest risk of infection is among dogs that reside in kennels or are exposed to transient groups of dogs, as in animal shelters or dog day care facilities. In some facilities, more than 40% of the dogs may be seropositive. Infected dogs from these high risk populations may introduce the virus into new areas. Currently, the H3N8 canine influenza virus does not appear to be common among household pets, with studies reporting seroprevalence rates less than 5%. In some areas, exposure rates have been low even in pets that participate in some types of gatherings (e.g., flyball tournaments). One study suggested that canine influenza is rare, if it exists at all, in Canada. In the province of Ontario, a survey found antibodies to the H3N8 virus in only one of 225 dogs in 2006. This dog was a greyhound that had come from a racetrack in Florida, and may have been infected there. More recently, no seropositive dogs were found among Canadian and U.S. dogs that participated in the 2010 Iditarod race.

During outbreaks among fully susceptible dogs in close contact (e.g., in kennels), the infection rate may approach 100%, and clinical signs in 60-80% of the dogs is not unusual. Most dogs are expected to develop the less severe form of the disease and recover; however, a more severe form with pneumonia occurs in a minority. The overall mortality rate is thought to be 1-5%, although some sources suggest that it might be as high as 8%. Secondary bacterial infections appear to contribute significantly to these deaths. Higher case fatality rates have been reported in small groups of greyhounds. At one Florida greyhound racetrack, the case fatality rate was 36%. More severe illness would also be expected in debilitated animals.

Canine influenza (H3N2)

Illnesses caused by the H3N2 canine influenza virus have been reported from veterinary hospitals, kennels and animal shelters in South Korea, China and Thailand. There is no known breed predilection; cases have been described in various species of dogs, as well as cats. Many of the reported clinical cases have been severe. In the initial report from Korea, only one of the 5 dogs seen at 3 veterinary clinics survived. Similarly, 2 of 4 cases in pet dogs diagnosed in China were fatal. During one explosive, severe outbreak at a Korean animal shelter, approximately 200 dogs and 50 cats showed signs of respiratory disease. The

morbidity rate was reported to be 100% in cats, while the case fatality rate was 25% in affected dogs, and 40% in cats. It is possible that other pathogens also contributed to this outbreak. At least one cat that died was co-infected with *Bordetella bronchiseptica*.

Studies have reported antibodies to the H3N2 canine influenza virus in cats and dogs with or without respiratory signs. Antibodies were found in 3.5% of serum samples collected from dogs in South Korea between 2005 and 2009, while studies from China have reported seroprevalence rates ranging from 3.5% to 33% in pet dogs. Antibodies to this virus were also found in 20% of stray dogs in animal shelters in China, and 12% of farmed dogs. One study reported that 16-33% of dogs living on poultry farms and near poultry markets were seropositive by HI assay, and 5-14% by microneutralization assay. Antibodies to the H3N2 canine influenza virus were also found in approximately 3% of pet cats and cats in colonies in South Korea, and 10% of pet cats and cats in animal shelters from northern China. While cross-reactivity with other influenza viruses can complicate serological studies, some have reported a pattern of reactivity that is higher to the H3N2 canine influenza virus than to H3 influenza viruses from other species.

Public Health

There are no reports of human infections with canine influenza viruses, although such infections are theoretically possible. As a precaution, physicians, veterinarians and others have been asked to report any cases of human influenza that seem to be linked to exposure to canine influenza. As a general practice, it is prudent for immunocompromised people, the elderly, young children and pregnant women to avoid contact with animals that are ill.

Internet Resources

American Animal Hospital Association (AAHA) Client Fact Sheet
http://secure.aahanet.org/eweb/dynamicpage.aspx?site=resources&webcode=CI_clientfactsheet

Cornell University College of Veterinary Medicine. Canine Influenza Virus (including testing, sample submission).
https://ahdc.vet.cornell.edu/news/civ.cfm

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

Public Health Agency of Canada. Pathogen Safety Data Sheets
http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php

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