Canine Influenza

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Importance

Canine influenza is an emerging disease. No influenza viruses circulated in dogs until genetic changes in an equine influenza virus allowed this virus to spread efficiently in the canine population. Canine influenza was first reported in racing greyhounds, and initially seemed to be confined to this breed. Beginning in 2004, outbreaks of respiratory disease occurred at greyhound kennels and racetracks in a number of U.S. states. The canine influenza virus was found to be responsible for some outbreaks, and is thought to have been involved in others. Serologic evidence suggests that this virus has been circulating among greyhounds since at least 1999. Recently, it has also caused respiratory disease in a variety of breeds in the general canine population. All dogs regardless of breed are now considered to be susceptible.

Because this is the first influenza virus to circulate in dogs, they are not expected to have any immunity to canine influenza. If the virus enters a kennel or other closed group, a high percentage of the dogs will probably become infected, and most of these dogs will be symptomatic. Approximately 20-25% of infected dogs are expected to remain asymptomatic, but can still shed the virus and disseminate the disease. Although most dogs have a milder form of canine influenza and recover, some may develop severe pneumonia. Deaths occur mainly in dogs with the severe form of disease; the mortality rate is thought to be 1-5% or slightly higher. Higher case fatality rates have been reported in small groups of greyhounds that developed hemorrhagic pneumonia during outbreaks.

In 2007, a different influenza virus caused an outbreak of canine respiratory disease in Korea. This virus appears to be entirely of avian origin, but can be transmitted between dogs. As of 2009, it has been reported only from a limited geographic area.

Etiology

The canine influenza virus is a member of the *Influenzavirus A* genus in the family Orthomyxoviridae. This genus contains many closely related influenza viruses that infect birds (avian influenza viruses), horses (equine influenza viruses), pigs (swine influenza viruses) and people (human influenza A viruses). Each of these viruses has a higher specificity for one species or related group of animals (e.g. birds). Equine influenza viruses, for example, typically infect only horses and other members of the Equidae. Occasionally, an influenza virus from one species infects a member of another species. Typically, the virus is poorly adapted to the new host and cannot be transmitted efficiently. For this reason, most of these infections remain limited to individual animals or small groups. However, in some instances, influenza viruses have been able to jump from one species to another. Although permanent adaptation to another species is uncommon, it is aided by two characteristics of influenza viruses: their high mutation rate and their ability to recombine with each other.

Influenza A viruses are classified into subtypes based on two surface antigens, the hemagglutinin (H) and neuraminidase (N) proteins. There are 16 hemagglutinin antigens (H1 to H16) and 9 neuraminidase antigens (N1 to N9), but only limited subtypes are found in each species of mammal. H3N8 viruses are currently the predominant subtype in horses. The canine influenza virus, which has the subtype H3N8, appears to have jumped directly from horses to dogs. This virus is considered to be a canine influenza virus because it has acquired the ability to spread from dog to dog. An analysis of the H3N8 canine influenza virus has demonstrated that it is most closely related to the H3N8 'Florida lineage' equine influenza virus that emerged in the early 1990s. There are four amino acid differences between the hemagglutinin proteins in the equine and canine viruses; these changes were probably important in adapting the virus to dogs. Although it is remotely possible that the canine influenza virus was repeatedly introduced into dogs from some other species, the evidence suggests that a single virus was transmitted whole from horses to dogs, as a one-time event. Recent studies show that the canine H3N8 influenza virus has now diverged considerably from the H3N8 equine influenza virus from which it originated, and appears to belong to a separate lineage.

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A second subtype, an H3N2 virus isolated in Korea, has the potential to become a second canine influenza virus. There is evidence that this virus may have been transmitted between dogs during an outbreak, and dog-to-dog transmission is reported to occur readily in experimentally infected dogs. At least three different isolates of this virus have been recovered. Unlike the H3N8 virus, the H3N2 virus seems to have originated in birds. The H3N2 viruses are reported to contain gene segments which may come from several different avian viruses. The source of the H3N2 virus is not known, but one possibility is that it originated in uncooked poultry products fed to dogs. One dog might also have been exposed at a poultry market.

There have been sporadic reports of other influenza viruses, including the high pathogenicity avian H5N1 virus, in dogs. However, these viruses have not been readily transmitted between dogs. For this reason, they are not considered to be canine influenza viruses. For example, an H3N8 influenza virus caused disease in dogs during an equine influenza outbreak in Australia in 2007; however, this virus does not seem to have become adapted to dogs, and this outbreak is considered to be equine influenza in dogs.

Species Affected

Canine influenza has been reported only in dogs. Although the H3N8 virus was first seen in greyhounds, all breeds are now considered to be susceptible. The H3N2 virus has not demonstrated any breed predilection. As of January 2009, no infections with H3N8 or H3N2 canine influenza viruses have been reported in other species, including humans.

Geographic Distribution

H3N8 canine influenza has been reported in the U.S. In 2004-2006, infections occurred in racing greyhounds in a number of states including Florida, Texas, Arkansas, Alabama, Arizona, West Virginia, Kansas, Iowa, Colorado, Rhode Island and Massachusetts. Infected pet dogs were first reported in Florida, but the H3N8 virus has since spread to other areas. This virus seems to spread unpredictably. It has apparently become established in some regions including Colorado, Florida and the New York City area (New York, New Jersey and Connecticut), but its persistence in other areas is uncertain. Although infected dogs have also been reported from several other states, the virus seems to have disappeared from some.

In the U.K., an H3N8 virus was responsible for an independent outbreak of respiratory disease in a foxhound kennel in 2002. Limited serologic evidence also suggests that some foxhounds were exposed to an H3N8 virus in 2003. These cases were caused by equine H3N8 viruses that apparently did not become established in the canine population.

H3N2 viruses have been reported only from Korea.

Transmission

In mammals, influenza viruses are usually transmitted in aerosols created by coughing and sneezing, and by contact with nasal discharges, either directly or on fomites. Close contact and closed environments favor transmission. Influenza viruses are relatively labile, but can persist for several hours in dried mucus.

Transmission of the canine influenza viruses between dogs appears to be similar. Both the H3N8 and H3N2 viruses are found in respiratory secretions; neither virus has been reported in feces. Dogs can shed the H3N8 virus for seven to 10 days after the onset of clinical signs. Approximately 20-25% of dogs remain asymptomatic; however, these dogs can also shed the virus. Dogs that were experimentally infected with H3N2 viruses shed these viruses in nasal secretions from the second to sixth day after inoculation.

Incubation Period

The incubation period for H3N8 canine influenza is approximately 2 to 5 days; most cases appear in 2 to 3 days. In dogs inoculated with H3N2 canine influenza virus, fever first appeared at 24 hours, and other clinical signs began 2 to 8 days after inoculation. Dogs that became ill after exposure to H3N2-inoculated dogs developed fever in 3 days and other clinical signs after 5 to 8 days.

Clinical Signs

Canine influenza is an emerging disease in dogs, and there is only limited information on the clinical signs. The most common presentation seen with H3N8 viruses is a mild respiratory disease that resembles infectious tracheobronchitis (kennel cough). In this form, an initial (usually low grade) fever is followed by a persistent cough and sometimes a purulent nasal discharge. The cough may be either soft and moist, or dry, and can last for up to 3 to 4 weeks regardless of treatment. In uncomplicated cases, dry coughs are more common. The purulent nasal discharge appears to resolve with antibiotics, suggesting that secondary bacterial infections may be important in this disease. Lethargy and anorexia are common. More severely affected dogs exhibit a high fever with an increased respiratory rate and other signs of pneumonia or bronchopneumonia.. Some dogs are found dead peracutely with evidence of hemorrhages in the respiratory tract; this syndrome has been seen in racing greyhounds, but does not seem to be prominent in pets. Asymptomatic seroconversion also occurs.

The only known outbreak of H3N2 canine influenza was characterized by severe respiratory disease with fever, nasal discharge, sneezing, coughing and anorexia. Four of five pet dogs seen at veterinary clinics died. Fever, sneezing, coughing and nasal discharges occurred in experimentally inoculated dogs, and severe pathologic changes were seen in the lungs.

Post Mortem Lesions

In fatal cases of H3N8 virus infection, hemorrhages may be found in the lungs, mediastinum and pleural cavity. The lungs may exhibit signs of severe pneumonia, and can be dark red to black. Fibrinous pleuritis can also be seen in some cases. On histologic examination, there may be tracheitis, bronchitis, bronchiolitis, and severe interstitial or bronchointerstitial pneumonia. There is limited information on the lesions found in mild cases. In experimentally infected puppies with this form, the bronchial lymph nodes were edematous, and cranioventral lung consolidation was rarely seen. The most severely affected puppies had small focal areas of pulmonary hemorrhage scattered throughout the lungs, but there was no evidence of severe hemorrhagic pneumonia.

In dogs that were inoculated with H3N2 viruses, multifocal to coalescing reddish consolidation was found in the lungs. The histopathologic lesions included severe multilobular or diffuse necrotizing tracheobronchitis, and severe multilobular bronchiolitis and alveolitis. Mild to moderate thickening of the alveolar septae was also seen. No lesions were found outside the respiratory tract.

Morbidity and Mortality

In mammals, the severity of an influenza virus infection usually varies with the dose and strain of virus and the host's immunity. In most species, uncomplicated influenza infections are typically 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 influenza symptoms, prolong recovery and result in complications such as pneumonia. Canine influenza is likely to share many of these characteristics.

Canine H3N8 influenza was first reported in racing greyhounds and, at first, appeared to be confined to this breed. Although this disease was first reported in 2004, new evidence suggests that the H3N8 virus may have been circulating in U.S. greyhound populations as early as 1999. Researchers have found antibodies to this virus in 33% of greyhound sera from 1999, and 1-44% of greyhound sera collected between 2000 and 2004. More recently, H3N8 canine influenza has been seen in a variety of breeds at veterinary clinics, animal shelters, rescue groups, pet stores and boarding kennels in several U.S. states. All dogs regardless of breed or age are now considered to be susceptible. The prevalence of this disease in the U.S. is not yet known. One study suggests 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. It had no recent history of respiratory disease.

Because dogs have not been exposed to the canine influenza virus before, most of the population is expected to be fully susceptible. Many cases have been linked to shelters, boarding kennels and other areas where dogs are in close proximity. In kennels, the infection rate may reach 100% and clinical signs often occur in 60-80% of the dogs infected. 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. Deaths typically occur in dogs with severe disease; the mortality rate is thought to be 1-5%, although some sources suggest that it may 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%. High case fatality rates are not expected in most canine populations; however, severe disease is more likely in dogs that are in poor condition or are concurrently exposed to other pathogens.

The H3N2 virus has been reported only from an outbreak at three veterinary hospitals and a kennel in South Korea. Cases were described in a miniature schnauzer, a cocker spaniel, a Yorkshire terrier and two Jindo dogs (a Korean breed of hunting dog), as well as 13 dogs of unknown breeds at an animal shelter. This disease appears to be relatively severe: only one of the five dogs seen at veterinary clinics survived. The fate of the dogs in the animal shelter was not stated.

Diagnosis

Clinical

Canine influenza should be suspected in dogs with a persistent cough; this disease often resembles infectious tracheobronchitis (kennel cough). In a kennel or other facility, the occurrence of clinical signs in many dogs is suggestive. Canine influenza is also a consideration in dogs with pneumonia and other, more severe respiratory signs.

Differential diagnosis

The differential diagnosis includes other respiratory diseases, particularly kennel cough.

Laboratory tests

At this time, serology and reverse transcription polymerase chain reaction (RT-PCR) assays are the most reliable methods for detecting H3N8 canine influenza. Hemagglutination inhibition is the most commonly used serologic test. Virus neutralization (microneutralization test) can also be done, but this test is usually too cumbersome for routine use. Antibodies may be present as soon as 6 to 8 days after the onset of disease.

RT-PCR is the most reliable method to detect the virus directly. This test can be used in live animals (swabs) or at necropsy. Virus isolation may also be successful in some dogs, during the early stages of disease before antibodies develop. 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. Virus isolation may fail to detect the virus in many infected dogs that do not die of the disease. Nevertheless, it is important to track genetic changes in this virus as it spreads in canine populations. For this reason, some laboratories may conduct virus isolation, at no cost, on samples positive by PCR. Antigen-capture ELISA tests do not seem to be reliable in individual dogs, probably because the amount of virus shed is low. However, these tests may be able to detect H3N8 canine influenza during outbreaks at kennels or other large facilities.

Little is known about diagnostic testing for the H3N2 virus, but virus isolation has been successful in some dogs. RT-PCR can also detect this virus. Serology is expected to be useful.

Samples to collect

Acute and convalescent serum samples, collected 2 to 3 weeks apart, should be submitted if possible. Since canine influenza is an emerging disease, most dogs are not expected to have pre-existing titers to the virus; however, single titers are still considered less useful. In live dogs, swabs should be submitted for RT-PCR. Nasal swabs are preferred. If possible, they should be taken no more than 3 to 4 days after the first signs of disease. Transtracheal washes may also be considered in some circumstances. Lung tissue samples should be collected for RT-PCR in dogs that have died.

The H3N8 canine influenza virus can sometimes be found in lung tissues taken at necropsy, but virus isolation is difficult in live dogs. Peak virus shedding is most likely to occur 2 to 5 days after infection. Samples taken in a dog that has had clinical signs for more than three days are unlikely to be successful. In experimental infections, nasal swabs have been more likely to yield virus than nasopharyngeal swabs.

Some H3N2 viruses were isolated from nasal swabs taken from dogs during an outbreak. In experimentally infected dogs, H3N2 viruses are shed in nasal secretions from one to six days after inoculation.

Treatment

Antibiotics appear to be important in the treatment of H3N8 canine influenza, which seems to be complicated by secondary bacterial infections in some cases. Broad-spectrum antibiotics are used in the severe form of disease. These antibiotics are also used to control the signs of secondary bacterial infections (e.g. a purulent nasal discharge) in the milder form. Supportive treatment including hydration is also important.

Recommended actions if canine influenza is suspected

Control

A conditionally licensed vaccine for dogs has been released in the U.S. Vaccines for other respiratory diseases, such as kennel cough, may help control pathogens that could become secondary invaders.

Influenza viruses, including canine influenza viruses, are readily killed by commonly used disinfectants. In general, influenza viruses are susceptible to a variety of disinfectants including 1% sodium hypochlorite, quaternary ammonium compounds, 70% ethanol, glutaraldehyde, formaldehyde and lipid solvents. They can also be inactivated by heat of 56°C (133°F) for a minimum of 30 minutes, as well as by radiation or low pH (pH 2).

Influenza viruses usually spread most readily when animals are gathered together. Good infection control practices will help protect dogs in kennels, boarding facilities, dog shows and similar situations. Cages, bowls and other fomites should be cleaned and disinfected between uses. Workers should wash their hands with soap and water after handling dogs or cleaning cages, and after contact with saliva, urine, feces or blood, as well as after entering or before leaving the facility. Clothing can be cleaned by washing it with detergent at normal laundry temperatures. Isolation protocols, including the use of disposable gloves, should be used for any dog that develops respiratory signs.

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 such as recent boarding. Veterinarians should use contagious disease protocols for all dogs with respiratory symptoms. This includes the isolation of infected dogs during diagnosis and treatment, and during hospitalization if it becomes necessary. It should be kept in mind that asymptomatically infected dogs are also expected to be contagious.

If an outbreak occurs at an establishment, a quarantine and the isolation of infected animals would reduce virus dissemination to the community and within the facility. Good hygiene can help prevent influenza viruses from spreading on fomites. Infected facilities should be cleaned and disinfected after the outbreak.

Public Health

There are no reports of human infections with canine influenza viruses, and no evidence that any species other than dogs can be infected. However, it may be theoretically possible for dogs to become a source of novel influenza virus transmission to humans. 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

American Veterinary Medical Association (AVMA). Control of Canine Influenza in Dogs
http://www.avma.org/public_health/influenza/canine_guidelines.asp**

Cornell University College of Veterinary Medicine. Canine Influenza Virus Detection, Sampling and Statistics
http://www.diaglab.vet.cornell.edu/issues/civ-stat.asp**
http://diaglab.vet.cornell.edu/issues/civ.asp#samp**

Cornell University College of Veterinary Medicine. Test Summary for Canine Influenza Virus in Dogs not Affiliated with Greyhound Racetracks
http://diaglab.vet.cornell.edu/issues/civ-stat.asp**

Public Health Agency of Canada. Material Safety Data Sheets
http://www.phac-aspc.gc.ca/msds-ftss/index.html

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