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 as a significant issue in dogs. A few infections were reported in dogs in the past, often during human flu pandemics or influenza outbreaks in other species, when exposures and awareness were both high. However, no influenza viruses were known to circulate in dogs until 2004-2006, when an H3N8 virus from horses caused outbreaks of severe respiratory disease among racing greyhounds in the U.S., killing some animals. This virus eventually began spreading among other dogs; however, the illness in these animals was milder and more typical of mammalian influenza, with the most common syndrome being a kennel cough-like upper respiratory disease with a persistent cough. A second canine influenza virus was recognized in 2007, when an H3N2 virus from birds caused an outbreak among dogs in South Korea. This virus, which may have first infected dogs around 2005, was subsequently reported in China, Thailand, the U.S. and Canada, and can also affect cats. While the initial reports from veterinary clinics and animal shelters in Asia described a high proportion of severe, life-threatening cases, subsequent findings suggest that most animals have a milder syndrome similar to H3N8 canine influenza. Both viruses spread most efficiently where groups of susceptible dogs are in close contact, and whether either virus will persist long-term in dogs is unclear.

Etiology

Canine influenza viruses are considered to be part of a diverse group of viral and bacterial agents which, alone or in combination, cause a syndrome known as canine infectious respiratory disease complex (CIRDC), infectious tracheobronchitis or kennel cough.

Canine influenza viruses belong to the species *influenza A virus* (genus *Alphainfluenzavirus*, family Orthomyxoviridae), a large group of highly variable viruses that are adapted to circulate in particular hosts, but can occasionally infect other animals. Most influenza A viruses are maintained in birds (avian influenza viruses), but a few circulate in mammals including people (human influenza A viruses), pigs (swine influenza viruses) and horses (equine influenza viruses). (Additional viruses circulate in bats, but do not seem to be transmitted to or from other species.) On rare occasions, influenza viruses can adapt to a new host species, either "whole" or after reassorting with another influenza virus.

Influenza A viruses are classified into subtypes (e.g., H3N2) based on two variable surface proteins, the hemagglutinin and neuraminidase. There are currently 18 recognized hemagglutinins (H1 to H18) and 11 neuraminidases (N1 to N11). These two proteins are major targets for the immune response, and there is ordinarily little or no cross-protection between different HA or NA types. Mutations cause gradual changes in a virus's HA and NA genes, a process called 'antigenic drift.' If the hemagglutinin and neuraminidase proteins change enough, a host's existing immune responses against that virus may no longer be protective. Genetic reassortment, which results from "re-shuffling" the 8 viral gene segments when two different viruses infect a single cell, can result in more rapid changes. Viruses can reassort whether they are adapted to the same host species or originally came from different hosts (e.g., an avian influenza virus reassorting with a canine influenza virus). These processes can cause two influenza viruses that were originally identical to diverge as they circulate. The high variability also means that two viruses with the same subtype (e.g., an H3N2 avian influenza virus and an H3N2 canine influenza virus) may be only distantly related.

Two influenza viruses, an H3N2 virus and an H3N8 virus, are currently maintained in dogs. The H3N8 canine influenza virus seems to have jumped "whole" from horses to dogs in North America, probably in the late 1990s or early 2000s. It is most closely related to the Florida lineage of H3N8 equine influenza viruses, but has diverged to the point where it no longer seems to replicate efficiently in horses. The H3N2 canine influenza virus, which has gene segments that may have come from several different avian influenza viruses, seems to have originated in birds. There is some evidence that this virus may have been present in dogs in South Korea as early as 2005 and in China in 2006. It has also produced a number of variants. Some H3N2 viruses isolated from

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dogs in Asia now have genes from other avian influenza viruses or H1N1 human influenza A viruses. A few reassortants that contain genes from H3N2 canine influenza viruses but have a different subtype (e.g., H3N1) have also been described in dogs in Asia. None of the latter viruses seem to be established or circulating in dogs, at present.

Influenza A viruses of horses, humans, birds and pigs can infect dogs sporadically, but are not maintained in canine populations. Sometimes they may spread between dogs in a group; however, sustained transmission has not been reported in canine populations, and they are not considered to be canine influenza viruses.

Species Affected

As of 2021, dogs are the only species known to be infected by H3N8 canine influenza viruses, except in laboratory experiments. There is almost no published research on the susceptibility of other canids, though one limited survey found no evidence that this virus circulates in wildlife in Pennsylvania. Its ability to replicate in horses appears to be greatly reduced: although horses can be infected experimentally, virus shedding was low or absent, and transmission to naive horses was inefficient. Horses did not become infected when kept in close contact with experimentally infected dogs. One group found viral nucleic acids in two cats by PCR but concluded that the cats were not infected, as they never seroconverted. In laboratory studies, the H3N8 canine influenza virus was not transmitted readily to chickens, turkeys or ducks, and it did not replicate well in pigs.

The H3N2 canine influenza virus is maintained in dogs, but it can also cause clinical cases in cats. Cats do not seem able to act as reservoir hosts. A study from Asia found antibodies to this virus in a small number of horses, and these antibodies correlated with dog contact; however, it is also possible that these horses were exposed to cross-reactive avian H3N2 viruses. Experimental infections have been established in ferrets, guinea pigs and mice, and ferrets and guinea pigs could transmit the virus to naive contacts in some, though not all, studies. One study found no evidence of virus replication in experimental inoculated pigs. Another group did report limited replication in the lungs of pigs; however, these animals had been inoculated intratracheally as well as intranasally, directly depositing the virus deeper in the respiratory tract and bypassing some innate defenses. Both studies found that pigs did not shed the virus or infect naive pigs in contact. There was no evidence for virus shedding in experimentally inoculated chickens or ducks.

Zoonotic potential

No human infections have been reported with either canine influenza virus, though such infections are theoretically possible. Among people who were in contact with H3N2 virus infected dogs in China, one of 50 pet owners had antibodies that reacted in a serological test with this virus, while 28 veterinary staff were seronegative. Cross-reactive antibodies (e.g., to avian H3 viruses) could not be ruled out in the seropositive individual.

Geographic Distribution

The H3N8 canine influenza virus has been detected, at least sporadically, in most states in the U.S. Its distribution is patchy, and it has disappeared from some areas after causing an outbreak. As of December 2021, outbreaks caused by the H3N2 canine influenza virus have been confirmed in Korea, China, Thailand, the U.S. and Canada. Some reports from Canada suggest that the virus did not persist there, and only one outbreak was documented in Thailand. A serological study found no evidence for this virus in Japan.

All reports from outside these areas have been based on serological surveys, which could be detecting cross-reactive antibodies to other viruses, and are not definitive. A study from Nigeria found antibodies to H3N8 viruses in some dogs, though there was no evidence for infection with H3N2 viruses. Antibodies to H3N8 viruses were found in a small number of dogs in China, including Hong Kong. A single study from Italy found antibodies to H3N2 viruses in 38% of dogs tested; however, most surveys of dogs in Europe found a low prevalence of antibodies (< 4%) against either influenza A virus. All attempts to detect canine influenza viruses by PCR in healthy or sick dogs in Europe were unsuccessful.

Infections with influenza A viruses not adapted to dogs can occur wherever these viruses are endemic. Some viruses, including human influenza viruses and H3N8 equine influenza viruses are cosmopolitan.

Transmission

Mammalian 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 canine influenza virus has been found in the respiratory secretions of both symptomatic and subclinically infected dogs. Overall, the titers of this virus appear to be low, and it does not seem to spread rapidly in the community. However, transmission can occur more efficiently where groups of susceptible dogs are in close contact, such as in a kennel. The H3N2 canine influenza virus might be transmitted more efficiently. It also seems to be shed longer, with some reports of intermittent virus isolation as long as 2-3 weeks during outbreaks at shelters, and detection by PCR up to 24 days. Treatment with glucocorticoids has been reported to prolong its shedding.

Cats and experimentally infected ferrets can shed the H3N2 canine influenza virus, though this was not consistent between studies in ferrets. Dogs infected with other influenza viruses (i.e., those not adapted to dogs) may or may not transmit them to others in close contact.

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 remain viable for less than 24-48 hours on most surfaces, and often seem to be infectious for a few minutes to hours in many environments. Nevertheless, some data indicate that they might survive longer on some fomites or under some conditions, for example when protected in feces. Some laboratory experiments suggest that avian influenza viruses and human influenza A viruses might persist for weeks or months in some types of water (e.g., distilled); however, they might be inactivated much faster in aquatic environments that contain normal microbial flora. Low temperatures and protection from sunlight enhance virus survival.

Disinfection

Influenza A viruses are susceptible to a wide variety of disinfectants including sodium hypochlorite, 60-95% ethanol, quaternary ammonium compounds, aldehydes (glutaraldehyde, formaldehyde), phenols, acids and iodides. Common household agents including 1% bleach, 10% malt vinegar or 0.01-0.1% dishwashing liquid in water ("washing up liquid"), as well as antimicrobial wipes, were found to destroy the viability of human influenza viruses, although hot water alone (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 often around 2-3 days, and is thought to range from about one to 5 days. It appears to be similar for the H3N2 virus, though respiratory signs did not appear until 8 days in some experimentally infected dogs. The incubation period was 2-7 days in cats experimentally infected with the latter virus.

Clinical Signs

Canine influenza (H3N8)

The most common presentation in H3N8 canine influenza is a mild illness typical of infectious tracheobronchitis (kennel cough) and some other upper respiratory diseases. An initial (usually low grade) fever may be followed by a persistent cough. The cough tends to be nonproductive and dry, in cases not complicated by co-infections, but it may also be soft and moist, and it can last for up to 3 weeks regardless of treatment. Other common clinical signs include nasal discharge, sneezing, ocular discharge, lethargy and anorexia, while diarrhea and/or vomiting have been reported infrequently. 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 is also possible.

More severely affected dogs exhibit a high fever with an increased respiratory rate and other signs of pneumonia or bronchopneumonia, as well as nonspecific signs of illness. 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)

Although dogs in early reports from South Korea and China were severely ill and deaths were common, it now appears that most dogs have mild to moderate respiratory illnesses similar to those caused by H3N8 viruses. Occasional severe cases and deaths have been seen, but seem to be infrequent, and often occur in dogs that are older, debilitated and/or have pre-existing illnesses. Subclinical infections also seem to occur.

Cats infected with this virus can also develop respiratory illnesses. During early outbreaks at two animal shelters in South Korea, the clinical signs included coughing, dyspnea, tachypnea and lethargy. As in dogs, a significant number of these infections were fatal. Co-infections appear to have played some role in at least one of these outbreaks. Milder cases and seropositive cats have since been reported in Asia. No fatalities were seen among cats at an animal shelter in Indiana (U.S.), where infected cats had signs of an upper respiratory infection (nasal discharge, congestion) and general malaise, as well as excessive salivation and "lip smacking," but quickly recovered. Cats experimentally infected with H3N2 canine influenza viruses developed a fever, lethargy and respiratory signs including coughing, sneezing, ocular and nasal discharge, conjunctivitis and abdominal breathing.

The clinical signs in experimentally infected ferrets ranged from minimal weight loss to respiratory and nonspecific signs (e.g., sneezing, fever, lethargy, anorexia). Some ferrets were asymptomatic. Experimentally infected guinea pigs remained asymptomatic but developed lung lesions, and mice were asymptomatic with minimal lung lesions.

Other influenza viruses in dogs

In the U.K., an H3N8 equine influenza virus caused a limited outbreak among foxhounds in 2002. The dogs developed bronchointerstitial pneumonia, with clinical signs of coughing, lethargy and weakness, which sometimes progressed to loss of consciousness. 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).

Natural or experimental human (H1N1 and H3N2) or avian influenza virus infections in dogs have ranged from asymptomatic or mild cases (e.g., transient fever, conjunctivitis or mild respiratory signs) to severe illnesses with respiratory signs, fever and other systemic signs.

Post Mortem Lesions

Canine influenza viruses commonly cause tracheitis and bronchitis, with some extension to the bronchioles. In some animals, the lungs may contain petechiae, areas of consolidation and other lesions consistent with viral pneumonia, especially later in the illness. Fatal cases caused by both H3N8 and H3N2 viruses seem to be characterized mainly by suppurative secondary bacterial pneumonia. However, hemorrhagic pneumonia was common in fatal H3N8 canine influenza cases in racing greyhounds, with hemorrhages in the lungs, mediastinum and pleural cavity. The lungs, which exhibited signs of severe pneumonia, were dark red to black in these animals. Some greyhounds also had fibrinous pleuritis.

The lesions appear to be similar in cats, but hemorrhagic pneumonia has not been reported.

Diagnostic Tests

Canine influenza can be diagnosed by detecting H3N8 or H3N2 viruses in nasal or pharyngeal samples from live dogs, or in tissue samples from the respiratory tract at necropsy. In one study of experimentally infected dogs, nasal swabs were more likely to yield H3N8 virus than nasopharyngeal swabs. Most clinical cases are diagnosed with RT-PCR tests, which are available for both viruses. Virus isolation can also be done, but it is unlikely to be successful in a dog that has had signs for more than a few days. Antigen-capture ELISA tests for influenza virus nucleoproteins do not seem to be reliable in individual dogs infected with H3N8 viruses, probably because the shedding of this virus is low, the timing of sample collection is not always optimal, and false positives are common. However, antigen ELISAs may be useful during investigations of outbreaks at kennels or other facilities. They might also have a role in detecting H3N2 viruses or other influenza viruses that are shed at higher levels.

Serological tests can be used for retrospective diagnosis or in animals with prolonged signs. Hemagglutination inhibition (HI) is considered the test of choice for detecting antibodies to the H3N8 virus. HI assays are also available for the H3N2 virus. Virus neutralization (microneutralization test) can be used, though it is too cumbersome for routine use. Although acute and convalescent titers are ideal, exposure is uncommon in some areas and a single sample collected more than 7 days after the onset of clinical signs may be suggestive. Cross-reactivity between the two canine influenza viruses is not likely to be an issue, as they are genetically distant; however, antibodies to equine H3N8 viruses may be detected in tests for H3N8 canine influenza, and antibodies to some H3N2 avian influenza viruses may react in tests for the H3N2 virus. In-house commercial ELISA tests can recognize antibodies to influenza A viruses in general; though these tests should be interpreted with caution in areas where exposure to human and/or avian influenza viruses is common.

Treatment

Treatment is supportive, and may include antibiotics to control secondary bacterial infections. The antiviral drugs (e.g., neuraminidase inhibitors) used in human influenza have not been tested in dogs. In people, 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 a sick dog is seen by a veterinarian.

Control

Disease reporting

Veterinarians who encounter or suspect canine influenza should follow their national and/or local guidelines for disease reporting. In the U.S., this disease is currently reportable in some U.S. states, but not others. Information about canine outbreaks is often disseminated even where there are no formal reporting requirements.

Prevention

Influenza viruses usually spread most readily where 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. Some shelters found that a 21-day isolation period seemed to result in better control of the H3N2 virus, which may be shed for prolonged periods, than either 7 or 14 days. A 28 day quarantine was employed during outbreaks in Canada.

Canine influenza vaccines are licensed for H3N2 viruses in South Korea and China, and for both H3N8 and H3N2 canine influenza in North America. One report noted that some of the dogs involved in H3N2 outbreaks in Canada had been recently vaccinated with both doses, raising questions about vaccine efficacy. In North America, vaccines appear to be particularly useful for dogs that regularly contact other dogs in facilities such as boarding kennels, daily care facilities, dog parks and dog shows.

Because a number of outbreaks in North America have been linked to imported dogs, particularly rescue dogs from Asia, improved screening and quarantines of these animals might be helpful.

Morbidity and Mortality

Uncomplicated infections with a host-adapted influenza virus tend to be associated with high morbidity, low mortality and rapid recovery. More severe disease and increased fatalities may be seen in very young, old or

debilitated animals. Secondary bacterial infections can exacerbate the clinical signs, prolong recovery and result in complications such as pneumonia. This pattern also seems to apply to the canine influenza viruses.

Canine influenza (H3N8)

Although H3N8 canine influenza was first reported in racing greyhounds, all breeds are susceptible. This virus circulated continuously in the U.S. for more than a decade, but it is now found at very low levels and appears to be restricted to a few geographic pockets. The greatest risk of infection is among dogs that reside in kennels or are exposed to transient dog populations, as in animal shelters, dog training classes or dog day care facilities; seroprevalence in household pets is typically less than 5%. During an outbreak among naive animals, the infection rate in a facility may approach 100% within days, and clinical signs in 60-80% of the dogs is not unusual. The group is often resistant to reintroduction of the virus after the outbreak, due to the high level of immunity.

Most dogs are expected to develop mild to moderate clinical signs and recover; however, a more severe form with pneumonia occurs in a minority, particularly dogs that are elderly, debilitated or have chronic diseases. The overall mortality rate in naive animals is thought to be 1-5% or lower. Secondary bacterial infections appear to contribute significantly to these deaths. Racing greyhounds had severe outbreaks with an unusual hemorrhagic form of the disease when the H3N8 virus first began to circulate, and the case fatality rates were high, with one Florida greyhound racetrack reporting a case fatality rate of 36%.

Canine influenza (H3N2)

The H3N2 canine influenza virus has no known breed predilection in dogs or cats. Many of the clinical cases reported initially from veterinary hospitals, kennels and animal shelters in Asia were severe, with a high case fatality rate. Morbidity rates in two South Korean animal shelters, where concurrent infections with other respiratory pathogens might have contributed to the illness, ranged from 47% to 100% in dogs and cats, while the case fatality rate was 23-25% in dogs and 22-40% in cats. Recent reports from both Asia and North America suggest that the currently circulating H3N3 viruses cause a disease similar to H3N8 canine influenza, though severe outbreaks are occasionally reported at some animal shelters or pet breeding facilities in China. Deaths have been uncommon in the U.S. and Canada, and typically occurred in elderly dogs with comorbidities. Reports and informal analyses from the North American outbreaks suggest a case fatality rate no higher than < 1% to 3%. One study found that experimentally infected beagles developed respiratory signs of varying severity, and there was one death, but beagles that became infected by contact with these dogs had only mild to relatively mild respiratory signs.

Like the H3N8 virus, the H3N2 virus spreads most readily among groups of dogs or cats in close contact. Studies from Asia have found antibodies to this virus in 1-33% of dogs, and 1-10% of cats. These rates tend to be higher among stray dogs in animal shelters, dogs raised for meat, and dogs living on poultry farms and near poultry markets than pets, though one study reported that 33% of pet dogs were seropositive. Most of the outbreaks in the U.S. and Canada appear to have began with introductions of the virus from Asia, often via rescue dogs, with the virus subsequently spreading within and between communities. These outbreaks generally faded out after a few months, probably because limited contact between groups of dogs prevented ongoing transmission. A 2015 study, which mainly examined outbreak areas in Indiana and Illinois, found antibodies to H3N2 virus in 2% of dogs (452 samples) and 9% of cats (67 samples).

Other viruses

Globally, surveillance of dogs and cats has found that a small percentage of these animals have antibodies to avian influenza viruses (with some studies suggesting a higher prevalence in cats), equine influenza viruses, swine influenza viruses and/or human influenza viruses. Reactivity to the currently circulating H1N1 human influenza viruses seems to be particularly high, up to 10% in some studies. However, only a few dogs or cats appear to have antibodies to H3N2 human influenza viruses.

Public Health

While there are no definitive reports of human infections with canine influenza viruses, zoonotic infections might be possible. 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 Veterinary MedicalAssociation (AVMA). Canine influenza. (includes client handout for AVMA members only)

Cornell University College of Veterinary Medicine. Canine Influenza Virus (including testing, sample submission).

The Merck Veterinary Manual

University of Florida. College of Veterinary Medicine. Maddie's Shelter Medicine Program. Disease Response in Animal Shelters

Maddie's Shelter Medicine Program. Article on vaccination and other resources on canine influenza for animal shelters

University of Wisconsin Shelter Medicine Program

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*Link is defunct

