

CANINE INFLUENZA: EPIDEMIOLOGY, CLINICAL DISEASE, DIAGNOSIS, TREATMENT, AND PREVENTION

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Epidemiology

Canine influenza is a highly contagious respiratory infection of dogs caused by influenza A subtype H3N8 virus. Canine influenza virus (CIV) was discovered in the USA as the cause of acute respiratory disease outbreaks involving thousands of greyhound dogs at 20 different race tracks in 8 states from 2003 to 2005.¹ Subsequently, ongoing surveillance jointly conducted by the University of Florida and Cornell University has identified thousands of dogs with laboratory-confirmed influenza infection in 30 states and the District of Columbia in the USA.¹⁻⁴ The virus is now enzootic in many communities in Colorado, Florida, Pennsylvania, New Jersey, and New York.

Dogs housed in different types of communal facilities such as kennels, shelters, pet stores, dog shows, and veterinary clinics are at highest risk for exposure to CIV. Canine influenza outbreaks reach epidemic proportions in facilities with high density and high turnover populations. Dogs of any age, breed, and health status are susceptible. CIV does not infect people, and there is no documentation that other species have become infected by exposure to dogs with canine influenza. Experimental studies have shown that horses are susceptible to CIV infection, but the infection induces either no or very mild clinical disease.⁵ Canine influenza does not have a seasonal pattern of occurrence.

Molecular analyses of CIV isolates support their origination from the interspecies transmission of equine influenza A H3N8 viruses from horses to dogs at some point prior to 2004. Viral adaptation to the dog has resulted in a canine-specific pathogen that replicates efficiently in the respiratory tract to cause clinical disease and is sustained in canine populations by dog-to-dog transmission.^{1,4} Since original discovery in the USA, equine influenza H3N8 viral infections have been reported in dogs in England⁶ and Australia,⁷ but there was no evidence of dog-to-dog transmission. Currently, there are no reports of canine influenza H3N8 cases outside of the U.S., but this may change as more investigations are conducted.

Transmission

Transmission is by oronasal contact with infected dogs or contaminated fomites, and by inhalation of aerosols generated by coughing and sneezing. The incubation period is 2 to 4 days.^{1,8,9} Peak virus shedding occurs during the preclinical incubation period and rapidly declines over the ensuing days to

cessation by day 7 to 10.^{1,8,9} A proportion of dogs have asymptomatic infection but shed virus and thus are contagious.^{1,4,8,9} Once virus shedding ceases, dogs are no longer contagious. All dogs in a facility should be considered exposed and a potential infectious risk, whether or not they have clinical disease. Important management strategies for reducing spread of canine influenza within a premise include isolation of sick and exposed dogs and institution of strict biosecurity measures for staff providing care.

Clinical Signs

Influenza virus replicates in mucosal epithelial cells lining the airways from the nose to the terminal airways, in bronchiole gland epithelium, and in pulmonary macrophages. Viral replication causes epithelial cell necrosis and destruction of the respiratory epithelial barrier, predisposing to secondary infections by a variety of commensal bacteria, including *Streptococcus spp*, *Staphylococcus spp*, *E. coli*, *Klebsiella*, *Pasteurella multocida*, and *Mycoplasma spp*.^{1,4} The primary viral infection initiates intense neutrophilic and monocytic inflammatory responses resulting in rhinitis, tracheitis, bronchitis, and bronchiolitis.^{1,4}

Because CIV is still a novel virus for most dogs, virtually all exposed dogs become infected; about 80% develop clinical disease while about 20% have subclinical infection.^{1,4} Clinical disease consists of acute onset of cough, sneezing, nasal discharge, and some ocular discharge.^{1,4,8,9} Cough is the predominant sign and typically persists for 2 to 3 weeks due to the intense inflammation. Secondary commensal bacterial infections contribute to development of mucopurulent nasal discharge and productive cough.^{1,4}

Most clinically affected dogs recover from influenza without complications; however, less than 20% progress to bronchopneumonia associated with virus-induced damage to lower airway epithelium and complicated by secondary bacterial infections.^{1,4} Pulmonary congestion, consolidation, and petechial hemorrhages have been described in experimentally infected dogs that developed pneumonia in the absence of secondary bacterial infections.^{1,9} Dogs with pneumonia have high fevers, inappetance, productive cough, and increased respiratory rate and effort. Pulmonary consolidation can cause respiratory distress and severe hypoxia.

Diagnosis

Canine influenza cannot be diagnosed based on clinical signs since the clinical spectrum overlaps with that due to other respiratory pathogens. Dogs without pneumonia have unremarkable complete blood cell counts and serum chemistry values. Dogs with secondary bacterial infections in the lower respiratory tract may have leukocytosis consisting of neutrophilia with a left shift. For dogs with pneumonia, thoracic radiograph findings range from mild bronchointerstitial infiltrates to consolidation of all lung lobes. Cultures of transtracheal, endotracheal, and bronchoalveolar lavages may yield a variety of gram negative or positive bacteria, and neutrophils are the predominant cell type on cytological examination.

Postmortem examination findings include pulmonary edema and congestion, epithelial necrosis and erosion in all airways, and suppurative rhinitis, tracheitis, bronchitis, bronchiolitis, and bronchopneumonia.^{1, 4}

Definitive diagnosis of canine influenza requires detection of virus in acutely ill dogs coupled with serology. Methods for virus detection include ELISA for antigen, RT-PCR for nucleic acid, and virus isolation.^{1, 3, 4} Successful virus detection by all 3 methods depends on sample collection during peak virus shedding early in the course of clinical disease. Nasal and pharyngeal swabs collected from dogs with clinical signs for <4 days can be tested for influenza A nucleoprotein using point-of-care ELISA kits available for diagnosis of human influenza A infections. While the kits detect CIV, the sensitivity is reduced by lower virus shedding in dogs compared to horses, pigs, and people. RT-PCR for influenza A matrix gene can detect very low amounts of virus on swabs, but false negatives occur due to the critical timing of sample collection. Serology is the most accurate and reliable diagnostic test for confirmation of CIV infection, especially in cases where the PCR test is negative but the index of suspicion is high.^{1, 3, 4} Paired acute (sick for <7 days) and convalescent (10 to 14 days later) serum samples are necessary for diagnosis of recent active infection based on seroconversion. Seroconversion is defined as a ≥ 4 -fold increase in CIV antibody titer between the acute and convalescent sample.

Treatment

Treatment consists mainly of supportive care based on clinical signs and laboratory tests. Although there is no specific antiviral treatment for canine influenza at this time, a variety of secondary bacterial infections may play a significant role, and antibiotics are indicated for dogs with fever, purulent nasal discharge, productive cough, and pneumonia. Antitussives are not very effective in reducing frequency and duration of coughing, and should not be used on dogs with productive cough.

Although canine influenza has a low mortality rate overall, pneumonia cases can be life-threatening if not managed aggressively in the hospital setting to maintain hydration, administer parenteral antibiotic therapy, and provide oxygen support. Ideally, antibiotic selection should be based on culture and sensitivity testing of lung washes. Empirical selection should include a broad spectrum combination of bactericidal antibiotics that provide 4-quadrant coverage. More severe cases of pneumonia with lung consolidation and hypoxia benefit greatly from oxygen supplementation and nebulization with corticosteroids.

Prevention

Influenza viral disease is best prevented by vaccination. In June 2009, the first canine influenza H3N8 vaccine for dogs (Intervet/Schering Plough Animal Health) was approved. The vaccine contains inactivated whole virus with adjuvant, and is intended as an aid in the control of disease associated with CIV infection. Although the vaccine may not prevent infection, efficacy trials have shown that vaccination

significantly reduces the severity and duration of clinical illness, including the incidence and severity of damage to the lungs. In addition, the vaccine reduces the amount of virus shed and shortens the shedding interval. This means that vaccinated dogs that become infected have less illness and are not as contagious to other dogs. The canine influenza vaccine is a “lifestyle” vaccine intended for dogs at risk for exposure while housed in communal facilities, particularly in communities where the virus is prevalent.

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