

Canine Influenza Virus: An Emerging Disease

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Introduction

Influenza type A viruses, which are enveloped RNA viruses, have long been among the most significant respiratory pathogens of humans, horses, birds, and swine. Recently, the emergence of an influenza virus in dogs has received widespread media attention. Influenza viruses are divided into subgroups and named on the basis of two surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA). There are 16 known HA subtypes and 9 known NA subtypes. Recombination of these segments of the genome allows for emergence of new viral subtypes, with occasional transmission of the viruses between species.

In January 2004, an outbreak of respiratory disease among racing Greyhounds in northeast Florida marked the emergence of a new canine-specific influenza virus. Fourteen of twenty-two affected dogs recovered after presenting with fever and coughing for 10-14 days. The remaining eight dogs died within hours from hemorrhage in the lungs, mediastinum, and pleural space. Post-mortem examination of these dogs revealed inflammation of the trachea and bronchi accompanied by bronchopneumonia. The respiratory epithelium and luminal airways were infiltrated with neutrophils and macrophages.¹

Nucleic acid sequencing of the canine influenza virus isolated from these Greyhounds showed a close relationship to the equine influenza H3N8 virus, with which it shared >96% sequence homology. The hemagglutinin, which plays a critical role in determining host species specificity, differs from equine influenza strains by only five amino acid residues.² Since all of the genes of the canine virus originated in equine influenza viruses, it was concluded that the entire viral genome had been transmitted from horse to dog. Direct transfer of an influenza virus from one species directly to another has been documented in other situations, including recent infection of humans with avian influenza virus H5N1. However, most direct transmissions between species don't result in sustained transmission in the new host species. In contrast, canine H3N8 influenza virus appears to have adapted to its host and is able to spread among dogs.³

Three months after the Florida outbreak, samples from asymptomatic dogs housed with those that had been ill showed that 93% (43/46) were seropositive for influenza. It appears that many cases of naturally acquired canine influenza virus result in subclinical illness. A small number of research dogs were experimentally infected via intranasal and intratracheal inoculation. Although exposure to the virus caused fever, viral shedding, seroconversion, and some histologic changes to the respiratory tract, severe respiratory disease was not observed.¹

Clinical presentation

In June 2004, a larger outbreak occurred in thousands of racing Greyhounds in six states. Although canine influenza was initially identified only in Greyhounds, they do not appear to be more susceptible than other breeds. A serological survey of shelter dogs in northeast Florida found that 97% of them were seropositive, so no genetic barriers prevent infection in the pet population. Since canine influenza virus is a new pathogen, a lack of protective immunity from vaccination or previous exposure means that all dogs should be considered susceptible.

Many infected dogs will show no clinical signs. Presenting clinical signs of canine influenza may vary, but the most consistent sign is a cough that persists for up to three weeks regardless of therapy. The cough may be either soft and moist, or it may be dry like kennel cough. This is often accompanied by an antibiotic-responsive purulent nasal discharge, suggesting that secondary bacterial infections may occur. The most severely affected dogs have a high fever (up to 106°F) with signs of pneumonia including dyspnea and tachypnea. The rate of mortality associated with pneumonia is estimated to be less than 5%.

In individual dogs, it may be difficult to differentiate influenza virus infections from infections with other kennel cough pathogens such as Bordetella bronchiseptica and parainfluenza virus.

Canine influenza is highly contagious in kennel settings, where infection rates may reach 100%. The incubation period for the virus is only 2-5 days. The virus is spread by aerosolized respiratory secretions as well as by fomites. Standard disinfectants including quaternary ammonium compounds and 10% bleach solutions should kill the virus. Appropriate isolation protocols for contagious diseases should be implemented in kennels, veterinary hospitals, and animal shelters when influenza is suspected. Dogs with the mild form of the disease may not require any treatment, although cough suppressants and antibiotics may be appropriate in some cases. Current treatment recommendations for severely affected dogs include fluid therapy and broad spectrum antibiotics for secondary bacterial infections. There may be a role for neuraminidase inhibitors like oseltamivir (Tamiflu®) that are used to treat human influenza cases.

Diagnostic testing

Currently, diagnostic testing for canine influenza virus requires detecting antibodies to the disease rather than virus isolation. Antibodies to the virus may be detected as early as seven days after onset of clinical signs. Ideally, acute samples obtained in the first week of illness and convalescent samples obtained two-three weeks later are analyzed as paired samples, with a four-fold increase in titers constituting seroconversion. Single serum samples from dogs that have recovered from a respiratory infection can be used to document previous exposure and the presence of the virus in the community. Nonfixed tissue samples from affected dogs can also be submitted for PCR analysis. Positive tests have been documented from about two dozen states by late 2006. Further information regarding sample submissions can be obtained from veterinary colleges at Cornell (www.diaglab.vet.cornell.edu) and the University of Florida (www.vetmed.ufl.edu/pr/nw_story/CanineFluSamplesProtocols.htm).

Much of the media attention devoted to canine influenza originates from concerns about other respiratory pathogens that have been transferred between species and resulted in human disease outbreaks. The risk of transmission of canine influenza virus to humans appears to be slim. Despite the persistence of H3N8 equine influenza virus in horses for over forty years, not a single case of human infection has been documented by the Centers for Disease Control.⁴ Surveillance by veterinarians will be necessary to obtain further information about the biological behavior of this emerging disease.

¹ Crawford PC, Dubovi EJ, Castleman WL et al. Transmission of equine influenza virus to dogs. *Science* 2005; 310: 482-485.

² Yoon KJ, Cooper VL, Harmon KM et al. Influenza virus infection in racing greyhounds. *Emerging Infectious Diseases* 2005; 11: 1974-1975.

³ Parrish CR and Kawaoka Y. The origins of new pandemic viruses: the acquisition of new host ranges by canine parvovirus and influenza A virus. *Ann Rev Microbiol* 2005; 59: 553-586.

⁴ Hampton T. Equine influenza virus jumps to canines. *J Am Medical Assoc* 2005; 294: 2015.