CANINE FLU: STATUS REPORT AND VACCINE UPDATE
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NATURAL HISTORY
In North America, canine flu is predominantly an H3N8 Type A influenza. This influenza jumped species from horses to dogs around 1999 or earlier, transferring the entire genome as a unit. It was recognized, and subsequently isolated, in a series of outbreaks that occurred in racing Greyhounds in the Southeast US in 2004.¹ Banked blood samples from Greyhounds that had been at tracks with respiratory disease outbreaks between 1999 and 2003 were later documented to exhibit seroreactivity to the H3N8 strain. Prior to that time, there was not a documented species-adapted influenza A of the dog. There has been no evidence of dog-to-human transmission of H3N8, nor was there evidence of horse-to-human transmission of this strain of influenza A prior to the existence of the canine-adapted version.

Curiously, H3N2 influenza appears to have jumped into the canine species on the Korean peninsula around the same time, likely through recombination events with various avian influenza viruses known to circulate in that area.² In 2015 an outbreak of canine flu in and around Chicago was documented to be the first cluster of H3N2 cases in North American dogs. A third canine influenza strain, H5N2, isolated in China can be spread from dog-to-dog, but sustained spread through pet populations has not yet been described. Influenza viruses are prone to recombination in co-infected hosts (termed "antigenic shift"), and this tendency is likely to continue to impact the emerging diversity of canine influenza strains.

Since influenza is a novel virus in the canine species, susceptibility is high. This is because the population has no native or historical immunity. This immunological naïveté is in contrast to species such as humans, birds and pigs, with our long-standing endemic history of influenza A infection. In such species a background low to moderate level of immunity persists, based on prior exposure to related strains of the same agent. Periodic antigenic shift and drift by the virus impact the efficacy of that historical immunity, and occasional epidemics result when the antigenic change is substantial.

Lacking background immunity, dogs as a species should be expected to experience an epidemic of flu, and indeed the disease has been spreading slowly through population clusters since 2004. However, not all highly contagious or highly prevalent diseases are highly lethal. The ongoing canine flu epidemic in North America is proving to exhibit lower mortality than had been initially feared.

Like other respiratory pathogens, canine influenza A is spread by respiratory secretions, respiratory aerosols, and fomites. The enveloped RNA virus is not highly durable in the environment, and can be readily killed by common disinfectants, including quaternary ammonium compounds and bleach. At this point in time, the infectivity rate seems to be at least 80%. To reiterate, this means that healthy adult dogs exposed to the virus will contract the infection in 80% of cases, because they have no historical immunity to any similar agent unless they have been deliberately vaccinated. The incubation period prior to the onset of clinical signs is 2-4 days, however, dogs are shedding contagious virus during this incubation period.

Once infected, the morbidity rate is approximately 75%. That is to say, of that 80% of dogs that actually became infected, ¾ will develop clinical signs. Conversely, up to 25% of naturally-infected dogs do not ever exhibit any clinical signs, although they may still be shedding the virus. Clinical signs begin to manifest while viral shedding by the infected dog is tapering. The typical clinical signs are fever, coughing, sneezing and malaise, which are indistinguishable from more classic causes of canine infectious tracheobronchitis (i.e., "kennel cough" or ITB) in an individual dog. Things that might raise suspicion for canine flu include rapid spread through a population of otherwise healthy and/or vaccinated adults, and potentially higher rates of fever. In most cases, the disease will be self-limiting,
or responsive to supportive care, and dogs will recover within 2-3 weeks. As with all canine ITB, complicating pneumonia is the most dangerous sequela, and the very old, the very young, or the previously unhealthy are at greatest risk of complications.

Early data suggested mortality rates were up to 10%. However, those estimates included the relatively large numbers of track greyhounds who died early in the discovery of disease, and mortality estimates have continued to be revised downward as the disease spreads through the pet population. At the time of writing, most authors estimate mortality at 1-5%. While the recent Chicago outbreak garnered a lot of media attention, there is no evidence that the H3N2 strain is more severe than the H3N8 strain. If popular press reports are accurate, over 1500 dogs were diagnosed with the disease and 6 deaths were reported, which would equal a mortality rate of 0.4%

DIAGNOSIS
The disease is indistinguishable from other canine ITB, is self-limiting in most cases, and has no definitive therapy. However, achieving a definitive diagnosis may still be of value, particularly in a shelter, kennel, or clinic outbreak. The UGA Athens Veterinary Diagnostic Laboratory (ugavetlab.org) offers a PCR test panel for canine flu and other agents of canine ITB, including *Bordetella bronchiseptica*, *Mycoplasma spp*, Canine adenovirus-2, Canine distemper, and Canine coronavirus. The sample of choice for this panel is nasal or pharyngeal swabs in a red top tube with a few drops of sterile saline, shipped priority overnight with ice packs.

PCR is a definitive rule in/rule out test for dogs showing acute clinical signs such as fever. However, false negative PCR results may occur after about one week of clinical disease. In such cases serologic testing (available through several commercial laboratories) is useful, provided two serum samples taken 2-3 weeks apart (first sample should be collected within a week of onset) are tested and a fourfold rise in titer is observed. Early in the course of the epidemic, a single positive titer was considered diagnostic because there was no background seropositivity in dogs. With the advent of a vaccine, and a growing population of dogs that have recovered from natural illness, a single positive titer is no longer considered sufficient to confirm the diagnosis.

THERAPY
Therapy is supportive as for all respiratory viruses, and complicating bacterial pneumonia will require the most aggressive care. Dogs should be allowed / encouraged to rest, and kept fed, hydrated, clean and warm. Some clinicians use prophylactic broad-spectrum antibiotic therapy in anticipation of secondary bacterial infection, particularly in very young, very old, or otherwise immunocompromised dogs. Racing Greyhounds in the early racetrack outbreaks experienced higher mortality; it is unclear whether this was due to breed-specific or husbandry-related factors. Aggressive supportive care including broad-spectrum antibiotic therapy may therefore be indicated in infected Greyhounds.

Oseltamivir has been used by some clinicians to treat this and other viral diseases of dogs. The author does not employ this agent for several reasons. In most instances of canine influenza, specific antiviral therapy would not be required because the disease is self-limiting. Limited safety or efficacy studies of oseltamivir in dogs exist, and no studies of oseltamivir in dogs infected with influenza exist. Finally, given the ongoing concern about pandemic human influenza, it seems prudent to minimize risk of induction of resistance by avoiding use of antiviral agents whenever possible.

PREVENTION
A killed virus adjuvanted vaccine (Nobivac® Canine Flu H3N8, Merck Animal Health), given as a two-dose initial series with an annual booster, was approved by the USDA for conditional release in May 2009 and granted full release in June 2010.

Experience would suggest that intranasal vaccine with a modified-live agent might be an efficacious way to induce protective local immunity that excludes the virus from the site of infection. However, because of concerns of recombination, which may be relevant to human influenza epidemiology, the USDA will not currently consider licensure of any MLV influenza products for canine use.
Limited studies have documented the efficacy of the killed H3N8 vaccine, and have largely been performed in laboratory settings. Overall, vaccinated dogs seroconverted after initial doses, demonstrated rising titers after booster doses, and exhibited minimum four-dilution anamnestic responses after challenge. Coughing was the predominant clinical sign in vaccinated and control dogs after challenge, and was more prevalent, subjectively more severe, and of longer duration in the unvaccinated controls. Results were similar whether the challenge strain was the homologous H3N8 vaccine strain, various field H3N8 strains, or co-challenge with H3N8 and Streptococcus zooepidemicus - in all cases, vaccinated dogs exhibited milder clinical signs for a shorter duration than controls. No studies have investigated the efficacy of the H3N8 vaccine against experimental or natural challenge with H3N2 virus.

Currently, H3N8 influenza vaccine is considered a non-core vaccine for dogs, and is recommended for a similar population of dogs that receive Bordetella bronchiseptica vaccines, that is, dogs that travel, board, show, or are regularly exposed to novel other dogs. While some clinicians have not chosen to vaccinate in regions of the country without a documented outbreak, it only takes a single infected dog to bring the virus into a new area, and most dogs are asymptomatic shedders for a period of time during the infection. Thus, the risk factors for Bordetella infection and canine influenza infection are the same in any region. In regions of the country where outbreaks have occurred, some kennels, dog parks and other canine facilities have begun to require the vaccine for dogs entering their populations.

Again, influenza viruses are prone to recombination (antigenic shift) and there is no research into H3N8 vaccine efficacy against novel or recombined strains such as H3N2. Influenza viruses are also prone to antigenic drift away from the original type, and recent evidence has confirmed that canine influenza virus does exhibit ongoing mutation during single infections. Ongoing investigation into vaccine efficacy against novel and emerging strains is warranted.

For more information, clients can be referred to the following AVMA site: https://www.avma.org/public/PetCare/Pages/CanineInfluenza.aspx

Practitioners can follow emerging developments with the AVMA: https://www.avma.org/KB/Resources/Reference/Pages/Canine-Influenza-Backgrounder.aspx

Testing is available at the UGA Athens and Tifton diagnostic laboratories (http://ugavetlab.org), other state veterinary laboratories and some commercial laboratories.

To contact the UGA Veterinary Diagnostic Laboratories, call 706-542-5568.

References