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NEWSLETTER

COVID-19 Coronavirus Pandemic and Veterinarians[©]

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In This Issue:

In the Spring 2020 issue of the NVL Newsletter, Dr. Hardy will discuss the SARS-CoV-2 induced COVID-19 coronavirus pandemic. This is truly a One Health crisis of unprecedented proportions involving humans and animals, especially pet cats, who recently were found to have been infected from their owners. Our laboratory is located in the epicenter New York/New Jersey of the Pandemic with the highest prevalence of infections, cases and deaths in our country. I have lost 2 high school friends already to this disease. This virus is impacting our civilization like no other event in modern history. Unless we develop an effective vaccine that will be accepted, AND utilized, by most people in the world, modern civilization may be changed forever.

Coronaviruses:

Coronaviruses are enveloped viruses with a singlestranded RNA genome and a nucleocapsid of helical symmetry (Figure 1).1 The name "coronavirus" is derived from the Ancient Greek (korone), meaning crown or halo, which refers to the characteristic appearance of the virus, as they have a fringe reminiscent of a crown or solar corona. Coronaviruses primarily infect the upper respiratory and gastrointestinal tract of mammals and birds. They also cause a range of diseases in farm animals and domesticated pets. In humans, the viruses cause respiratory infections, including the common cold, which are typically mild, though rarer forms such as SARS (including the one causing COVID-19) and MERS can be lethal. They are found in numerous animal species as well as humans who have 7 known coronaviruses.

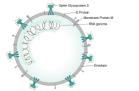


Figure 1. Wikipedia attribution: BySPQR10Bintealtaf-Own work, CC BY-SA 4.0 no alteration.

The Pandemic:

The Origin: Dr. Li Wenliang was a Chinese ophthalmologist who worked at Wuhan Central Hospital, Wuhan, the capital of China's Hubei province. He warned his colleagues, in December 2019, about a possible outbreak of an illness that resembled severe acute respiratory syndrome (SARS).² He was the whistleblower when his warnings were made public and he was admonished for them. His parents became infected with SARS-CoV-2, but later recovered. He returned

to work, but contracted the virus from one of his patients who he treated for glaucoma. He died from the disease on February 7, 2020, at the age of 33. However, these events, a cover-up, delayed the recognition of the significance of this virus and allowed the spread to occur unchecked for some time. The possible origin of SARS-CoV-2 is the Horseshoe bat coronavirus through an intermediate host, likely the pangolin (the most trafficked animal in the world), then into a person at the Huanan Seafood Wholesale Market in Huanan, China that sold wild animals as food (Figure 2).³





Figure 2. Attributions: Horseshoe bat, Aditya Joshi Creative Commons Wikipedia, Pangolin, Piekfrosh Creative Commons Wikipedia

Nomenclature:

The World Health Organization (WHO) announced in February 2020 that **COVID-19 is the official name of the disease.**⁴ WHO explained that CO stands for corona, VI for virus and D for disease, while 19 is for when the outbreak was first identified: December 31, 2019. The name had been chosen to avoid references to a specific geographical location (e.g. China), animal species or group of people, in line with international recommendations for naming aimed at preventing stigmatization.

SARS-CoV-2 (The Virus)

The cause of the disease COVID-19 is **the virus named Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2)**.⁵ The virus uses the receptor binding domain (RBD) on human cells, called ACE2 (angiotensin-converting enzyme 2), through high affinity binding to its S protein of the viral spikes (Figure 1). This high affinity makes the virus highly contagious.

COVID-19 (The Disease)

The World Health Organization (WHO) declared the 2019–20 coronavirus outbreak a Public Health Emergency of International Concern on January 30, 2020 and a pandemic on March 11, 2020. Local transmission of the virus has been recorded in many countries across all six WHO regions. The mains signs are fever (88%), dry cough (68%) fatigue (38%) and shortness of breath (19%). Other symptoms may include muscle pain, diarrhea, sore throat, loss of smell and taste and abdominal pain. The time from exposure to onset of symptoms is typically around 5 days, but may range from 2 to 14 days.⁶ While the majority of cases result in mild symptoms, some progress to viral pneumonia and multi-organ failure. As of April 12, 2020, more than 1.88 million cases have been reported in more than 200 countries and territories, resulting in 117,569 deaths.⁷ More than 400,000 people have recovered so far.

The virus is mainly spread between people during close contact, often via small droplets produced during coughing, sneezing, or talking. The droplets are produced when breathing out, they usually fall to the ground or surfaces rather than being infectious over large distances. People may also become infected by touching a contaminated surface and then their face. The virus can survive on surfaces for various times depending on the type of surface, some as long as 3-5 days. Transmission can occur before, during and even after clinical symptoms.

The standard method of diagnosis of infection is by real-time reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab. Chest CT imaging may also be helpful for diagnosis of disease in individuals where there is a high suspicion of infection based on symptoms and risk factors.

Recommended measures to prevent infection include frequent hand washing, maintaining physical distance from others (especially from those with symptoms), covering coughs and sneezes with a tissue or inner elbow, keeping unwashed hands away from the face and disinfection of surfaces with liquids containing at least 70% alcohol. The use of masks is now recommended for all people. Currently, there is no vaccine or antiviral treatment for COVID-19.

One Health:

The One Health movement is very relevant at this time as numerous animals carry their own coronaviruses and several, especially from bats, are zoonotic and have already been transmitted to humans causing severe epidemics (SARS and MERS).

Veterinary Medicine:

A study of domestic animals inoculated with the SARS-CoV-2 found that cats and ferrets appear to be "highly susceptible" to the virus, while dogs appear to be less susceptible, with lower levels of viral replication. The study failed to find evidence of viral replication in pigs, ducks, and chickens.⁸

Cats

In addition to their 2 known feline coronaviruses, FECoV and FIPV, cats have recently been shown to be very susceptible to infection by SARS-CoV-2 virus both by experimental infection and through natural transmission from possible COVID-19 owners and/or other infected cats.



Older people and cats are more susceptible to SARS-CoV-2

Cat SARS-CoV-19 Transmission Studies

Experimental Transmission Study:

The first study investigated the replication of SARS-CoV-2 in cats.⁸ Seven outbred subadult cats, aged 6-9 months, were inoculated intranasally with 10⁵ PFU of SARS-CoV-2 (CTan-H strain). Three cats were placed in separate cages within an isolator. In order to monitor possible respiratory droplet transmission, an uninfected cat was placed in a cage adjacent to each of the 3 inoculated cats within each isolator.

In the aerosol transmission of uninoculated cats, viral RNA was detected in the nasal turbinate of one animal, in the soft palates, tonsils, tracheas, lungs, and small intestine of the other 2 uninoculated cats that were euthanized on day 3 p.i. In the animals that were euthanized on day 6 p.i., viral RNA was found in the nasal turbinates, soft palates, and tonsils of both animals, in the trachea of one animal, and in the small intestine of the other. However, viral RNA was not present in any of the lung samples from either of these animals. Infectious virus SARS-CoV-2 (CTan-H) was recovered from the viral RNA-positive nasal turbinates, soft palates, tonsils, tracheas, and lungs of these subadult cats, but not from the viral RNA-positive small intestines.

In the transmission study, viral RNA was detected in the feces of two virus-inoculated cats on day 3 p.i., and in all three virus-inoculated subadult cats on day 5 p.i.. Viral RNA was detected in the feces of one exposed cat on day 3 p.i.. The pair of subadult cats with viral RNA-positive feces were euthanized on day 11 p.i., and viral RNA was detected in the soft palate and tonsils of the virus-inoculated animals and in the nasal turbinate, soft palate, tonsils, and trachea of the exposed animal, indicating that respiratory droplet transmission had occurred in this pair of cats. The other pair of animals were euthanized on day 12 p.i., and viral RNA was found in the tonsils of 1 of the virus-inoculated subadult cat, in the nasal turbinate, soft palate, tonsils, and trachea of the other virusinoculated subadult cat, but was not detected in any organs or tissues of the two exposed subadult cats. Antibodies against SARS-CoV-2 were detected in all 3 virus-inoculated subadult cats and 1 exposed cat by ELISA and neutralization assays.

The transmission experiment was replicated in studies with kittens (juvenile cats aged 2–3 months). Histopathologic studies performed on samples from the virus-inoculated juvenile cats that died or euthanized on day 3 p.i., revealed massive lesions in the nasal and tracheal mucosa epitheliums, and lungs. **These results indicate that SARS-CoV-2 can replicate efficiently in kittens, with younger cats being more permissive and, perhaps more importantly, the virus can transmit between cats via the airborne route**.

Natural Transmission Observations:

A recently released (as a preprint, non-peerreviewed study by the senior author with a publication record in major international leading scientific journals- Science) using serological tests of pet and stray cats from Wuhan. China, the city where the pandemic began.9 The infection of SARS-CoV-2 in cats was investigated by serology. A cohort of serum samples was obtained from cats in Wuhan, including 102 samples after the COVID-19 outbreak, and 39 negative control samples from **before** the outbreak who were used for determining the negative baseline OD reading for the ELISA tests. 15 of 102 (14.7%) cat sera collected after the outbreak were seropositive for the receptor binding domain (RBD) of the SARS-CoV-2 virus by ELISA and by western blot (to confirm the specify of the ELISA tests). Among these positive samples, 11 also had SARS-CoV-2 neutralizing antibody titers ranging from 1:20 to 1:1080. Three of the pet cats, with high neutralizing antibody titers, were owned by people with COVID-19 disease. This study demonstrated that the human SARS-CoV-2 virus infected pet and stray cats in Wuhan during the outbreak. No serological crossreactivity was detected between the SARS-CoV-2 and type I or II feline infectious peritonitis virus (FIPV).

Humans appear to be capable of spreading the SARS-CoV-2 to some other animals, a reverse zoonosis. The Bronx Zoo confirmed that a tiger had tested positive for SARS-CoV-2, with the zoo saying it believed the animal caught the infection from a known infected employee. Meanwhile, 2 pet cats in Hong Kong tested positive for the virus after being in contact with SARS-CoV-2 patients. Similarly, a cat in Belgium was infected from its owner, who fell ill with COVID-19, after traveling to northern Italy.

These are a monumental findings for veterinarians since infected cats may be able to act as SARS-CoV-2 reservoirs, vectors, and fomites and may be able to transmit the virus back to susceptible people (reverse zoonosis), including their owners, veterinarians and their clinic staffs. It should be noted, that no known transmission from cats to people has yet been reported, however these finding have only been known for several weeks and no studies have yet investigated this possibility.

Dogs

The same experimental inoculation transmission study described previously in cats was repeated in dogs. The replication and transmission of SARS-CoV-2 in dogs was evaluated.8 Five 3-month-old beagles were intranasally inoculated with 105 PFU of CTan-H, and housed with two uninoculated beagles in a room. Viral RNA was detected in the rectal swabs of two virus-inoculated dogs on day 2 p.i., and in the rectal swab of one dog on day 6 p.i.. Infectious virus was not detected in any swabs collected from these dogs. Two virusinoculated dogs seroconverted; the other two virus-inoculated dogs and the two contact dogs were all seronegative for SARS-CoV-2. These results indicate that dogs have low susceptibility to SARS-CoV-2. However, 2 pet dogs tested positive who were owned by SARS-CoV-2 infected people in Hong Kong.

Veterinary Organizations:

American Veterinary Medical Association According to the American Veterinary Medical Association (AVMA), there is "little to no evidence" that cats become ill if infected with the new coronavirus, and "no evidence that those that may be naturally infected spread (the virus) to other pets or people." (Editor's Note- this is outdated and incorrect, SARS-CoV-2 infected cats do show typical COVID-19 (disease) signs and can transmit the SARS-CoV-2 by aerosol to other cats.⁸

British Veterinary Association

In a statement, the president of the British Veterinary Association, said cat owners who were self-isolating or displaying symptoms of COVID-19 should stop their pets from leaving the house. According to the BVA "There is no evidence that pets can pass Covid-19 to their owners."

Australian Veterinary Association

The Australian Veterinary Association also advised cat owners to keep pets within households affected by COVID-19 if they had been exposed to a human case.

Pet Owners Questions: Ouestions:



Can cats and dogs transmit SARS-CoV-2 to us? Can fleas and ticks transmit SARS-CoV-2 amongst cats and dogs or to us? Is there a test for SARS-CoV-2 for cats and dogs? Pet owners have questions but we veterinarians don't have the answers yet so we must be cautious.

Current Status:

There are excellent sources of information regarding the pandemic. I feel the Johns Hopkins University is overall the best with 2 excellent sites: <u>https://coronavirus.jhu.edu</u>, and https://www.hopkinsmedicine.org/coronavirus/.

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Conclusion: Veterinarians should work to limit this pandemic and safeguard their patients, clients and employees with sound scientific programs. Assuming that infected cats cannot transmit the virus to people may be premature.