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Can pets transmit Covid-19 infection?

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In the past couple of months various reports of SARS-CoV-2 or Covid-19 infection in domestic animals has become a common concern for many veterinarians and their clients around the world. Most coronavirus infections in companion animals cause primarily gastrointestinal disease with few exceptions including infectious bronchitis virus in birds, hepatitis virus in mice and canine respiratory coronavirus in dogs (Erles *et al.*, 2003). The mutation rate of coronaviruses (CoV) is higher than other single stranded RNA viruses (Su *et al.*, 2016), and results in an increase of genetic recombination and the production of novel CoVs of high genomic diversity and unpredictable virulence (Su *et al.*, 2016). Its potential for cross-species transmission and its variety in zoonotic reservoirs has already resulted in the emergence of highly pathogenic human SARS-CoV in 2002 and MERS-CoV in 2013 (Peiris *et al.*, 2003; Raj *et al.*, 2014) and it is a matter of time, not if but when there will be another interspecies transmission outbreak.

The first case in a domestic animal was a geriatric Pomeranian dog that tested positive to the SARS-CoV-2 or Covid-19 virus at the end of February 2020 (AFCD, 2020a). Later in mid-March a younger 2-year-old German shepherd tested positive too (AFCD, 2020c), and a third case was reported by the Government of the Hong Kong Special Administrative Region (GHKSAR) at the end of March in a cat that tested positive to Covid-19 (GHKSAR, 2020a).

All these three cases reported in Hong Kong belonged to people that had tested positive to Covid-19 and as a consequence they were examined by the Agriculture, Fisheries and Conservation Department (AFCD) but none of the three pets showed any clinical signs. Genetic sequencing similarities found by the AFCD and the School of Public Health of the HKU from infected pet owners and their pets further supported a human to animal transmission.

All pets tested at the AFCD had samples from oral, nasal and rectal origin as carried out routinely in human studies (W. Wang *et al.*, 2020). The positive results reported were on a reverse transcription polymerase chain reaction (RT-PCR) test, regarded the most sensitive test for the diagnosis of Covid-19 (Y. Wang *et al.*, 2020).

Samples tested weak positive to Covid-19 in several separate tests over a period of time. The persistent positive PCR results confirmed and suggested true infection as contamination was avoided keeping the pets separated in government kennels.

Experts from the School of Public Health University of Hong Kong, the College of Veterinary Medicine City University of Hong Kong and the World Organization for Animal Health concurred these results were consistent with a true infection (AFCD, 2020b).

The GHKSAR confirmed in late March a positive serology at the WHO laboratory reference at the University of Hong Kong (HKU) on the first patient, the geriatric Pomeranian that had previously been negative (GHKSAR, 2020b).

Testing before the body has time to create antibodies since antibody formation may take 14 days to be present in serum. A weak infection can additionally cause a negative serology as seen with other CoV infections in humans. The creation of antibodies against the virus suggests an immune response from the dog and further supports a true infection caused by human to animal transmission.

Culture testing results were negative in the Pomeranian but resulted positive in nasal swabs of the German Shepherd, however, there was no transmission from the positive dog to another dog that lived in the same household and was negative on RT-PCR.

All three Hong Kong reported cases eventually cleared the viral infection as suggested by negative follow up RT-PCR testing, meaning viral RNA copies were not identified above detection levels. Culture and serology tests for the positive cat in Hong Kong are pending. As for the 17th of April the AFCD had conducted test on 52 pets animals including 30 dogs, 18 cats and 2 hamsters of which only two dogs and one cat had tested positive on RT-PCR.

Another report was released in late March regarding an infection with Covid-19 in a cat tested at the University of Liege, Belgium. The cat was diagnosed positive after RNA was found in vomit and stool that was owned by a positive Covid-19 owner as in the cases reported in Hong Kong. The cat was reported to have clinical signs but it is unknown whether they were attributable to the virus itself or to a concurrent illness. No isolation of virus was reported and serology tests are pending. No conclusions can be made until more information is released.

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Early in April a 4 year-old tiger was also reported to have tested positive to Covid-19 in New York, USA. Other wild felines in the same zoo were reported to show clinical signs but no RT-PCRs were conducted in the other tigers. It is feasible they might have also been infected with SARS-CoV-2, however without PCR testing or serology it is questionable, and it remains unconfirmed whether there was an association between the clinical signs observed and Covid-19 infection. All wild felines have been since reported to be improving.

The latest reported cases in animals are 2 cats that tested positive for SARS-CoV-2 in New York in late April, released by the U.S. Department of Agriculture and federal Centers for Disease Control and Prevention. The cats were from different areas of the state and both had mild clinical signs but were expected to make a full recovery. A positive Covid-19 individual owned one of the cats but the other positive cat was not associated to an infected or ill individual. It was suggested that mildly ill or asymptomatic contact or household members might have transmitted the disease. The USDA still recommends against routine testing of animals, as the occurrence is rare (CDC, 2020).

Despite the positive natural infections reported now worldwide, a veterinary diagnostic company has conducted about 4000 tests in canine and felines that have tested all negative at the time they were reported (IDEXX, 2020). A possible reason might be that natural infection would not occur in these pets unless they had been in contact with infected humans as was the case in all other positive reported pets.

A recently published paper reports different species being inoculated with high viral loads resulting in both clinical lesions and infection of one control cat that was placed together with experimentally infected cats. Both inoculated cats and an exposed control cat had detectable viral RNA as well as antibodies detected on an ELISA and neutralization assay (Shi *et al.*, 2020). The same experimental infection approach was used in dogs. Dogs were not able to transmit the disease when kennelled together with control subjects and did not seroconvert, indicating low susceptibility to SARS-CoV-2 as it happened with ducks, chicken and pigs. Ferrets were however able to transmit the infection, developed lesions and all had antibodies. Although this is very important information, the results of this study should be carefully interpreted. The animals in this study were not naturally infected and received high viral loads so they do not reflect the naturally weaker infections so far seen in infected domestic animals where virus isolation was negative and transmission amongst same species has not been reported.

In another preprint, 15 cats were reported seropositive from 141 samples of cats from Wuhan of which 32 had been taken previous to the outbreak and 102 had been taken after the outbreak (Zhang *et al.*, 2020). All the positive results were from the post-outbreak sampling suggesting a human to animal infection. Only 3 out of the 15 cats were owned by Covid-19 diagnosed infected patients and they had the highest neutralization titers. The other 12 positive cat samples were taken from cat hospitals or from stray cats. The source of infection for these cats is unknown and one could speculate whether other infected cats, infected people or fomites might have been the potential sources.

A more recent preprint has suggested that dogs and cats are more susceptible to infection with SARS-CoV-2 and that they could transmit the disease to other animals in contact with them specially cats (Shen *et al.*, 2020). The authors based their statement based on their findings of high binding affinity of SARS-CoV-2 to ACE2 domain. According to their result the affinity for binding was highest in chimpanzees (even higher than humans), followed by cats, cattle, monkeys and dogs amongst other animals. They even speculated that considering the widespread of stray cats in Wuhan they could have served as intermediate hosts of SARS-CoV-2 (Shen *et al.*, 2020).

Transmission from human to animals appears to occur in some viral infections like influenza and we have observed it happening with SARS-CoV and SARS-CoV-2 too when close contact occurs between infected humans and their pets. Preventive measures when handling pets should be taken to avoid transmission if a human is diagnosed with Covid-19, similarly to what is suggested amongst humans. Despite the proved human to animal transmission, a cross-species jump is still a rare occurrence. Transmission amongst pets in a natural setting is unlikely and has yet not been reported. Further research will help us understand better the zoonotic risks of SARS-CoV-2. Although preventive measures to avoid contact between infected individuals are recommended, there is no evidence pets can infect humans and is yet to be proved that they can transmit the disease to other pets in natural occurring infections.

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