

# Determining the Role of Natural SARS-CoV-2 Infection in the Death of Ten Domestic Pets

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## Abstract

Transmission of SARS-CoV-2, the virus that causes COVID-19, from people to companion animals has been reported globally. Between March 2020 and January 2021, the United States reported 94 companion animals with SARS-CoV-2. While most animals with SARS-CoV-2 have mild illness, 10 animals (5 dogs, 5 cats) died around the time of SARS-CoV-2 diagnosis. In one dog, histopathologic changes suggest SARS-CoV-2 exacerbated a severe chronic respiratory disease and contributed to death. In one cat, SARS-CoV-2 was associated with histopathologic changes suggesting the virus caused clinical signs that resulted in euthanasia. In the remaining eight animals, SARS-CoV-2 infection was an incidental finding (4 dogs, 4 cats). This report provides evidence that in rare circumstances, SARS-CoV-2 can contribute to or cause death in companion animals with underlying conditions.

## Main Text

SARS-CoV-2, the virus that causes COVID-19, is believed to have originated in horseshoe bats and emerged in the human population in late 2019, possibly through an intermediate host (1-3). Viral spillover from people into animal populations has occurred naturally throughout the globe in farmed mink, zoo animals including big cats and great apes, and companion animals (4, 5). Along with farmed mink, companion animals (i.e., dogs and cats) are the most commonly infected animal group, and are primarily infected by owners with COVID-19 (5). Nearly all companion animals infected with SARS-CoV-2 have been asymptomatic or have developed mild illness (6-9).

Severe illness due to SARS-CoV-2 infection has not been established in companion animals. Four companion animals positive for SARS-CoV-2 outside of the US are known to have died: a dog in the Netherlands, two dogs in Germany, and a cat in Spain (5). The role of SARS-CoV-2 in the dog deaths remain unknown. Post-mortem investigation of the cat in Spain cat implicated a pre-existing cardiac condition as the cause of death (10).

In the United States, approximately 3,625 animals were tested between March 2020 and January 2021. Of these, 94 of these companion animals (cats and dogs) were confirmed positive for SARS-CoV-2 (11). While most of these animals were subclinical or mildly ill, 10 (10.6%) companion animals died or were euthanized around the time of SARS-CoV-2 diagnosis. The purpose of this case series is to examine the characteristics of these companion animals and determine if their deaths were attributable to SARS-CoV-2.

## Results

A standardized algorithm was developed (Figure 1) and applied to each case. All animals reported met the United States Department of Agriculture's (USDA) SARS-CoV-2 confirmed positive case definition for animals (12). Cycle threshold (Ct) values are from real-time (RT) PCR using CDC's N target assay (13).

### Case 1

On April 28, an owner sought veterinary care for a 7-year-old male German Shepherd dog showing lethargy, labored breathing, decreased appetite, and weight loss of 30 pounds since mid-April. A chest radiograph suggested an enlarged heart, but an electrocardiogram was unremarkable. The dog's owner had been diagnosed with COVID-19 on April 21.

On May 15 and with no improvement, the dog presented to a second veterinarian with tachypnea and severe pallor of the mucus membranes. Bloodwork revealed severe non-regenerative anemia (red blood cell [RBC] 1.67 M/ $\mu$ L, reference range [RR]: 5.39 - 8.70 M/ $\mu$ L) and thrombocytopenia (54 K/ $\mu$ L, RR: 143 - 448 K/ $\mu$ L). White blood cell (WBC) count was within normal limits (9.92 G/l) but had a predominance of monocytes (54.5%). A screening test for heartworm disease and tick-borne pathogens was negative. Nasal swabs collected on May 15 and 20 were positive for SARS-CoV-2 RNA (RT-PCR; Ct 31) and negative, respectively. Serum collected on May 15 and 20 detected virus neutralizing antibodies (1:512). Prednisone and doxycycline were administered. The owner reported immediate improvement, with increased appetite and energy.

Over the next several weeks, the dog developed urinary incontinence, hematuria, hematemesis, and worsening dyspnea. Bloodwork on June 21 showed continued severe non-regenerative anemia, an increasing WBC count (72 G/l) with a predominance of monocytes (80%). Large, immature blastic cells, suggestive of a hemic neoplasia, were found on manual differentiation. The dog was euthanized on July 11. A necropsy was not performed. Based on laboratory results and clinical course, the cause of death was consistent with a hemic neoplasia such as acute lymphoid leukemia or lymphoma. This animal had clinical signs attributed to other disease processes (Figure 1, 1.i.), and had severe co-morbidities (Figure 1. 2a.i.). Therefore, SARS-CoV-2 infection was concluded to have been an incidental finding (Table 1).

### Case 2

On June 19, a 6-year-old male, neutered Boxer mix dog acutely developed seizures and hypersalivation. Both owners had developed symptoms (June 11 and 13) and tested positive for SARS-CoV-2 (June 12 and 15).

The dog was presented to a veterinary clinic on June 20 and was euthanized on June 21 after failing to improve with medical therapy. Upon learning that owners had been diagnosed with COVID-19, a nasal swab for SARS-CoV-2 testing was collected post-mortem and confirmed positive by RT-PCR (Ct 27). A necropsy performed on June 24 revealed an intracranial Schwannoma with regionally extensive encephalomalacia and neovascularization involving the optic nerve and overlying brain. Minimal rhinitis and palatitis were also noted; however, the dog did not show respiratory signs. The cause of death was attributed to intracranial Schwannoma and acute secondary hemorrhage. This animal had clinical signs attributed to other disease processes (Figure 1, 1.i.), and had severe co-morbidities (Figure 1. 2a.i.). SARS-CoV-2 was determined to be an incidental finding (Table 1).

### Case 3

On June 22, an 11-year-old male neutered domestic short-hair (DSH) cat developed dyspnea. On June 24, the cat was presented to a veterinary clinic. No diagnostics were performed, no treatments were attempted, and the owner was instructed to return if the clinical signs did not resolve. Between June 7 and June 14, all four persons in the household had developed febrile illness and tested positive for COVID-19.

On June 24, the cat's dyspnea worsened, and it was taken to an emergency clinic where clinicians noted tachypnea, hypothermia, and a heart murmur. Thoracic radiographs revealed no pneumonia or other abnormalities. Cardiac ultrasound showed bilateral markedly thickened myocardium and left atrial enlargement, consistent with hypertrophic cardiomyopathy (HCM). While hospitalized on June 25, the cat remained laterally recumbent with poor mentation. The cat died later that day; necropsy was not performed. After veterinary staff were informed that the animal came from a household that had people with COVID-19, nasal swabs were collected post-mortem and were positive for SARS-CoV-2 by RT-PCR (Ct 34). A standard respiratory panel was positive for *Mycoplasma felis*. Since clinical signs and cause of death were attributed to HCM, SARS-CoV-2 was concluded to be an incidental finding (Figure 1, 1.i. and 2a.i.; Table 1).

#### **Case 4**

On July 13, a 9-year-old female spayed Boxer-mix dog developed rear leg paresis. Radiographs were consistent with spinal disc disease or spinal neoplasia. At the request of the owner, who had tested positive for SARS-CoV-2 on July 20, a nasal swab was collected by the veterinarian on July 22 and tested positive for SARS-CoV-2 by RT-PCR (Ct 30). The dog was euthanized on August 5 due to hind limb plegia, with a presumptive diagnosis of intervertebral disc disease. Necropsy was not performed. A second nasal sample collected by the veterinarian post-mortem tested positive by RT-PCR (Ct  $\geq$  37), and serum was positive for virus neutralizing antibodies. SARS-CoV-2 infection was determined to be an incidental finding, as the dog showed no clinical signs consistent with SARS-CoV-2 (Figure 1, 1.i.) and was euthanized for unrelated reasons (Figure 1, 2a.i.; Table 1).

#### **Case 5**

On August 3, an 8-year-old Newfoundland dog developed acute respiratory distress and pyrexia (temperature: 105.2°F) and presented to a veterinary clinic. Owners reported that the dog was normal that morning. The dog's condition deteriorated over 12 hours, resulting in referral to an emergency hospital, where clinicians noted respiratory distress, weakness, tachypnea, tachycardia, and pyrexia (temperature: 104.8°F). Thoracic radiographs showed a severe alveolar pattern in the right caudal lung fields. Oxygen saturation was 70% while receiving supplemental oxygen. Bloodwork was consistent with metabolic acidosis. The dog arrested that evening and could not be resuscitated. One of the dog's owners had become symptomatic for COVID-19 on July 6 and tested positive on July 13.

Initial gross and histological post-mortem examination identified acute pneumonia, necrotizing rhinitis, mild hemothorax, mild to moderate right atrial and ventricular chamber dilatation, and chronic focal mural ulceration in the urinary bladder. Due to a COVID-19 positive household member, a respiratory panel and SARS-CoV-2 RT-PCR were run on nasal swabs collected post-mortem and were negative for all targets except for SARS-CoV-2 (Ct 31-36). Formalin-fixed paraffin-embedded (FFPE) sections of lung and nasal turbinates were negative for SARS-CoV-2 by RT-PCR and immunohistochemistry (IHC) at CDC's Infectious Diseases Pathology Branch (IDPB). *Escherichia coli* was isolated by culture from lung and spleen, and neutrophilic alveolar infiltrate was appreciated histologically. Gram-negative rods were seen within inflammation in the lungs, and IHC stains for *E. coli* were positive on lung tissue. These histopathology results were consistent with pneumonia without evidence of a viral component.

This dog had clinical signs consistent with SARS-CoV-2 infection (Figure 1, 1.ii.), but the primary cause of death was attributed to bacterial bronchopneumonia (Figure 1, 2b.i.) and there was no evidence of virus in critical organs (Figure 1, 3a.i.). SARS-CoV-2 was determined to be an incidental finding (Table 1).

#### **Case 6**

On September 24, a 5-year-old male neutered DSH cat with a recent history of upper respiratory signs developed neurologic abnormalities (head pressing and seizures) and weakness. The cat received one dose of clindamycin but became unresponsive and died at home on September 25. A household member had tested positive for SARS-CoV-2 on September 18.

A necropsy revealed nasal discharge, pulmonary congestion and edema. Nasal and oral swabs were positive for SARS-CoV-2 (Ct 25-29) and a virus neutralization assay was positive (1:128). Fresh lung tissue was positive by RT-PCR (Ct 37). FFPE lung and tracheal tissues were positive by RT-PCR for SARS-CoV-2 at CDC IDPB. All tissues were negative by SARS-CoV-2 IHC. Histopathology showed suppurative meningoencephalitis, lymphoplasmacytic tracheitis, and mild myocardial disarray. In situ hybridization (ISH) for SARS-CoV-2 was performed, which showed sparse staining in the tracheal submucosal glands, and no staining in other tissues (lung, brain, spleen, liver, muscle). Histopathological changes suggestive of a viral infection were not observed in lung tissue. Broad-range 16S rRNA gene PCR assays for bacterial detection in brain were indeterminate. Assays aimed at identifying another infectious cause of the meningoencephalitis were negative.

This cat had respiratory signs consistent with SARS-CoV-2 infection (Figure 1, 1.ii.), a significant co-morbidity (suppurative meningoencephalitis) (Figure 1, 2b.i.), and evidence of SARS-CoV-2 in lung tissue (Figure 1, 3a.ii.) but without associated histopathologic lesions (Figure 1, 4a.i.). SARS-CoV-2 was considered the cause of tracheitis but incidental to the cause of death, which was attributed to suppurative meningoencephalitis (Table 1).

#### **Case 7**

On October 2, a 16-year-old male neutered DSH cat presented for evaluation of increased respiratory effort beginning in late September. The cat was treated with cefovecin and methylprednisolone. A respiratory panel was negative, and an oropharyngeal swab was positive for SARS-CoV-2 (Ct 28). On October 4, the owner reported improvement, but respiratory signs returned October 10. On October 13, the cat presented at a veterinary hospital with respiratory distress and

paradoxical breathing and was euthanized. Additional nasal, oropharyngeal, and rectal swabs, as well as heart, lung, and liver tissue samples were collected. The owner had tested positive for SARS-CoV-2 on September 18.

A post-mortem oropharyngeal swab and frozen nasal passage and lung tissue were positive for SARS-CoV-2 by RT-PCR (Ct 30-36); heart and liver specimens were negative. Molecular evidence of SARS-CoV-2 was not appreciated in five blocks of FFPE lung tissue evaluated at CDC IDPB. Histologically, moderate multifocal cardiomyocyte hypertrophy and disarray with degeneration, necrosis, and severe mineralization and fibrosis was seen in the heart. In the lungs, mild to moderate multifocal alveolar histiocytosis and interstitial fibrosis with edema, congestion, and hemorrhage was evident. Gross and histologic findings in the heart were consistent with HCM, and lung lesions were consistent with heart failure. The cat had clinical signs consistent with SARS-CoV-2 infection (Figure 1, 1.ii.), a severe co-morbidity (Figure 1, 2b.i.), and presence of virus in critical tissues (Figure 1, 3a.ii.) but without associated histopathologic lesions (Figure 1, 4a.i.). The cause of death was attributed to HCM with subsequent heart failure; SARS-CoV-2 was determined to be an incidental finding (Table 1).

### **Case 8**

On January 1, a 3-year-old male neutered DSH cat began vomiting and vocalizing in the litterbox. No respiratory signs were reported, and the animal was previously healthy. The owner did not take the animal for veterinary evaluation and elected to monitor overnight at home. The cat became weaker and died at home the next morning. The cat was brought to the veterinary hospital on January 2 for necropsy and cremation. Gross necropsy showed a urinary obstruction.

Two household members were symptomatic and recently confirmed positive for SARS-CoV-2. A nasal swab collected from the cat at necropsy was presumptive positive for SARS-CoV-2 via RT-PCR (Ct 29) on January 4 and confirmed positive via RT-PCR at USDA National Veterinary Services Laboratories (NVSL) (Ct 30) on January 11. Lung tissue was RT-PCR negative for SARS-CoV-2 on January 11 at NVSL.

SARS-CoV-2 infection was determined to be an incidental finding, as the cat showed no clinical signs consistent with SARS-CoV-2 infection (Figure 1, 1.i.), and necropsy findings suggested morbidity and mortality could be explained by urinary blockage (Figure 1, 2a.i.). Additionally, lung tissue was negative for SARS-CoV-2 by RT-PCR.

### **Case 9**

Beginning in March 2020, an eight-year-old male neutered Shepherd mix dog developed increased respiratory rate and effort. These signs initially resolved without treatment but reappeared on approximately June 12. One owner became symptomatic on June 21 and tested positive for SARS-CoV-2 on a sample collected on June 24.

The dog was presented to a veterinarian on June 21. Thoracic radiographs showed a bronchointerstitial to alveolar pattern. The dog's condition later deteriorated, and he was presented to an emergency hospital for dyspnea and cyanosis on June 23. Bronchoalveolar lavage (BAL) culture was positive for *Corynebacterium*, computed tomography showed chronic, diffuse pulmonary interstitial infiltrates with resultant cylindrical bronchiectasis, initial bloodwork was unremarkable (only mild neutrophilia noted), and bronchoscopy showed diffusely vascular and hyperemic airways and multiple, small blood clots in small airways. Antibiotics (ampicillin/sulbactam and enrofloxacin), corticosteroids, and supplemental oxygen were administered.

On June 26, veterinarians learned that the dog's owner had been diagnosed with COVID-19, and pursued SARS-CoV-2 testing. Based on the clinical picture, diagnostics, imaging, BAL culture, and the lack of response to therapy, the clinicians suspected end-stage lung disease (interstitial fibrosis or a poorly exfoliative neoplasia) that had been exacerbated by an acute infection. The dog failed to improve with treatment and was euthanized on July 2.

A respiratory PCR panel performed on the nasal swab collected on June 26 was negative for common causes of respiratory illness and positive for SARS-CoV-2 by RT-PCR (Ct 21). Histologic examination of formalin-fixed lung tissues revealed severe, chronic lymphoplasmacytic bronchointerstitial pneumonia with marked interstitial fibrosis and bronchiolar squamous metaplasia consistent with chronic, severe lung disease. One section showed features of proliferative and organizing diffuse alveolar damage, with patchy type II pneumocyte hyperplasia and occasional fibroblastic proliferations; these findings suggest repair from a recent infection on the background of severe chronic lung disease. SARS-CoV-2 was detected in RNA extracted from FFPE tissue in one of three sections of lung by RT-PCR. However, viral antigen was not detected by IHC or ISH in the respiratory tissues.

This animal had clinical signs consistent with SARS-CoV-2 infection (Figure 1, 1.ii), significant comorbidities (Figure 1, 2b.i.), presence of SARS-CoV-2 in critical tissues (Figure 1, 3a.ii.), and associated histopathologic changes (Figure 1, 4a.ii.); therefore, the final determination was that acute SARS-CoV-2 infection contributed to this animal's death, but the primary cause was chronic interstitial lung disease.

### **Case 10**

On December 10, a 4-year-old male neutered domestic medium hair cat became lethargic and inappetent. On December 13, the cat began to show signs of respiratory distress, and was seen at three veterinary clinics. On December 15, the owner elected euthanasia due to the cat's rapid, progressive clinical deterioration. Both household members tested positive for COVID-19 on December 5 and 21.

A necropsy was performed. Nasal, tracheal, oropharyngeal, and rectal swabs collected on December 18 were positive for SARS-CoV-2 by RT-PCR (Ct 14-16). On histopathologic examination, bronchointerstitial pneumonia, acute myocardial degeneration and necrosis, and mild HCM were appreciated (14). A necropsy was performed. Nasal, tracheal, oropharyngeal, and rectal swabs collected on December 18 were positive for SARS-CoV-2 by RT-PCR (Ct 14-16). On histopathologic examination, bronchointerstitial pneumonia, acute myocardial degeneration and necrosis, and mild HCM were appreciated (14). Live virus was isolated from nasal, tracheal, oropharyngeal, and rectal swabs, as well as heart and lung tissue. Both ISH and IHC were positive. A feline respiratory panel was positive for *Mycoplasma felis*. This cat had clinical signs consistent with COVID-19 (Figure 1, 1.ii.), sub-clinical co-morbidities (mild HCM) (2b.ii.), evidence of

SARS-CoV-2 in critical tissues (Figure 1, 3b.ii.), and histopathological changes attributed to SARS-CoV-2 in critical tissues (Figure 1, 4b.ii) (14). Therefore, infection with SARS-CoV-2 was determined to be primary reason for the animal's euthanasia.

## Discussion

SARS-CoV-2 infections in companion animals are thought to result in mild illness or asymptomatic infection. In the United States, from March 2020 to January 2021, 11% (10/94) of confirmed SARS-CoV-2-positive companion animals died during or shortly after diagnosis. One Health investigations were conducted by public health and animal health officials, in consultation with attending veterinarians and pathologists, to characterize clinical illness and determine the role of SARS-CoV-2 in the clinical outcome of these 10 animals. An algorithm was developed to standardize assignment of the role of SARS-CoV-2 in these deaths (Figure 1). SARS-CoV-2 was determined to be a contributing factor in the death of one dog and the primary cause of clinical signs that led to humane euthanasia for one cat, the first such reports in companion animals with natural infection globally.

CDC recommends testing for SARS-CoV-2 in companion animals with an epidemiologic link to people with COVID-19 and that show clinical signs consistent with SARS-CoV-2 infection (15). Four cases included in this case series did not fit this testing criteria; the animals had no signs consistent with SARS-CoV-2 infection. These animals had significant comorbidities that fully explained their clinical signs and death. Owners, veterinarians, and health officials should carefully consider the purpose of testing for SARS-CoV-2 in domestic animals, as there are currently no pathogen-specific therapies. These findings support other research describing subclinical animal infections with SARS-CoV-2. The clinical relevance of a SARS-CoV-2 diagnosis in a critically ill animal should be cautiously interpreted.

Significant comorbidities appreciated in these cases include HCM, severe chronic lung disease, spinal neoplasia or disc disease, hemic neoplasia, intracranial Schwannoma, bacterial bronchopneumonia, urinary obstruction, and suppurative meningoencephalitis. Despite most cases having severe comorbidities and epidemiologic links to COVID-19 positive owners, SARS-CoV-2 was determined to play a role in only two deaths. The only pet that was concluded to have died as a result of SARS-CoV-2 infection (Case 10) was only 4 years old and had no significant health conditions predisposing it to severe disease. In humans, the vast majority of human deaths occur in persons with significant underlying health conditions, but apparently healthy people can succumb to infection (16). HCM was appreciated in several of the cats in this case series. The significance of this correlation has yet to be established. Improvements in surveillance for infections and thorough evaluation of cases with severe outcomes will improve our understanding of the range of health impacts in companion animals.

Full necropsies were conducted for six animals, and a partial necropsy was performed on a seventh. Determination of the role of acute infections like SARS-CoV-2 is difficult in animals with severe underlying health conditions without extensive post-mortem evaluation and diagnostic testing. Necropsy and advanced detection methods necessary to characterize the virus' effects, such as ISH and IHC specific for SARS-CoV-2 require specialized equipment, facilities, and personnel (17). Veterinarians or owners who suspect that SARS-CoV-2 may have contributed to severe illness in an animal, with consistent clinical signs and exposure, should immediately notify animal health and public health officials to facilitate further investigation (18, 19). In some investigations, additional testing has been made possible through collaboration with and support from the U.S. Food and Drug Administration's Veterinary Laboratory Investigation and Response Network (Vet-LIRN) laboratories (20).

Of the six cases (2 dogs, 4 cats) in which tissues were evaluated histologically, three had viral lesions in respiratory and cardiac tissues, including the trachea, lungs, and heart. Rhinitis and tracheitis were each appreciated in two animals. It is unclear if rhinitis was caused by SARS-CoV-2 or was pre-existing and favored transmission. While SARS-CoV-2 was found in lung tissue of four animals, it was not consistently found in all lung lobes tested, or positive results were not repeatable. This has been observed in humans and highlights the importance of adequate tissue sampling (17). Histopathologic changes in the lung and upper airway tissue seen in cases 7 and 8 had shared features appreciated in feline SARS-CoV-2 challenge studies. However, these changes were not consistently detected. Animals that fit the testing criteria should be thoroughly evaluated similarly to the process described here.

This case series highlights several challenges of determining the role of natural SARS-CoV-2 infection in the clinical outcomes of companion animals, and the importance of assessing clinical signs in light of comorbidities, necropsy results, and histopathologic and tissue staining results. Not all animals in this case series with severe outcomes had clinical signs consistent with SARS-CoV-2 infection. Most animals had significant comorbidities affecting clinical course, necropsy findings, and tissues evaluation. In animals with non-specific clinical signs, necropsy, or histopathologic changes, advanced diagnostic techniques helped identify changes attributable to virus presence in the tissue rather than detection due to viremia or cross-contamination. Limitations of diagnostic tests must be considered, as virus may be unevenly or sparsely distributed in tissue. Histopathologic changes were not appreciated in all animals with natural infection and severity varied, perhaps due to differences in dose, inoculation route, or genetic factors associated with species or purpose bred laboratory animals evaluated in challenge studies. More research is needed to further evaluate and characterize the clinical and histologic manifestations of natural SARS-CoV-2 infection in companion animals.

## Conclusion

One dog had clinical and histopathologic evidence suggesting SARS-CoV-2 infection could have exacerbated a pre-existing chronic, severe lung disease, leading to the animal's death. One cat had no known significant pre-existing conditions that would pre-dispose the animal to a severe infection, yet the virus caused clinical signs and severe pathology that led to euthanasia. These are the first known instances of a direct histopathologic link between SARS-CoV-2 infection in a companion animal and severe clinical outcomes globally. At the time of writing, over 100 dogs and cats have been confirmed to be infected with this virus in the United States, and serological surveys indicate that 10% - 47% of pets living with owners with COVID-19 may develop antibodies to the virus (21). Despite apparently frequent human-to-pet infection, only two animals have been found to have died or been euthanized as a direct result of SARS-CoV-2 infection. Human-to-pet infections are significantly under-detected, and many pet infections are asymptomatic or self-resolving (21). However, in apparently rare instances, SARS-CoV-2 can cause severe outcomes in dogs and cats, irrespective of their health status. These cases highlight the importance of routine

data collection, longitudinal testing, and necropsies to learn more about the role of SARS-CoV-2 in companion animals. In cases detailed above, additional ante- and post-mortem diagnostics identified other conditions as the cause of the clinical signs for all but two of these deceased pets. Close collaboration among the treating veterinarian, state animal and public health officials, diagnostic laboratories, and federal partners using a One Health approach is essential to investigate these cases thoroughly.

## Declarations

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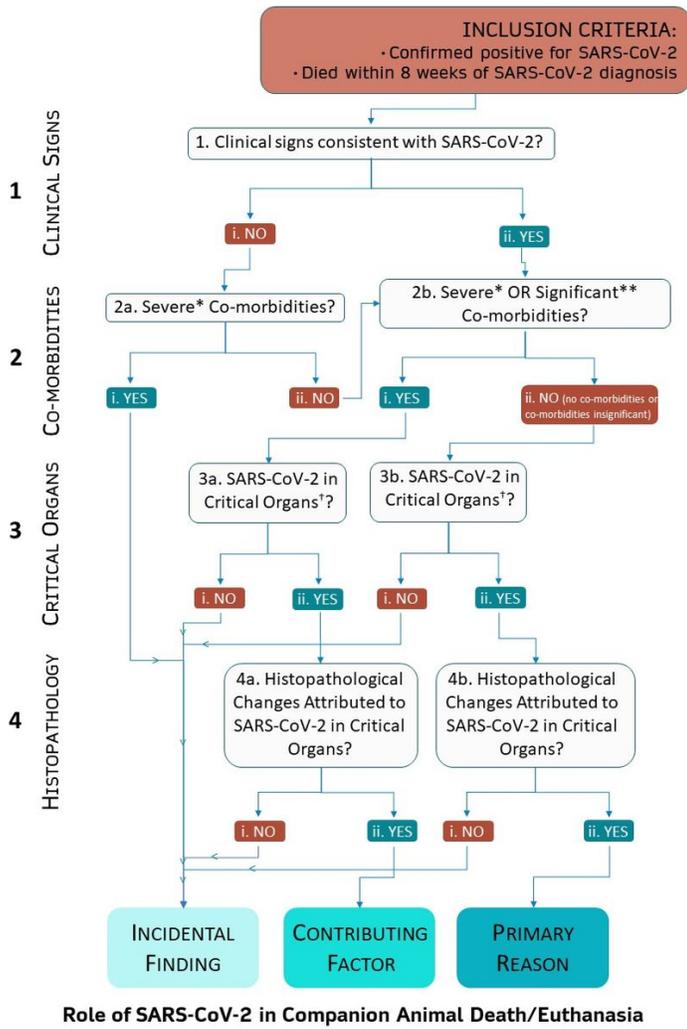
## Table

**Table 1.** Summary of case findings for five dogs and five cats that died or were euthanized shortly after SARS-CoV-2 diagnosis. All animals were confirmed positive for SARS-CoV-2 using USDA's case definition for SARS-CoV-2 in animals (12).

Case #	Breed	Age (Yrs.)	Co-morbidities	Clinical Onset Date	Confirmatory Diagnosis Report Date (mm/dd/yy)	Death Date	Primary Reason for Death	Necropsy?	Algorithm Interpretation*
1	Canine, German Shepherd Dog	7	Hemic neoplasia, most consistent with acute lymphoblastic leukemia	4/15/20	5/21/20	7/11/20	Severe anemia	No	1.i.; 2a.i.
2	Canine, Boxer mix	6	Schwannoma	6/19/20	6/25/20	6/21/20	Intracranial Schwannoma	Yes	1.i.; 2a.i.
3	Feline, Domestic shorthair	11	Hypertrophic cardiomyopathy	6/22/20	7/2/20	6/25/20	Hypertrophic cardiomyopathy	No	1.i.; 2a.i.
4	Canine, Boxer	9	Disc disease or spinal neoplasia	6/19/20	8/3/20	8/5/20	Disc disease or spinal neoplasia	No	1.i.; 2a.i.
5	Canine, Newfoundland	8	Chronic allergies, bacterial bronchopneumonia	8/3/20	8/7/20	8/3/20	Bacterial bronchopneumonia, possible sepsis	Yes	1.ii.; 2b.i.; 3a.i.
6	Feline, Domestic shorthair	5	Meningoencephalitis	9/24/20	10/2/20	9/25/20	Severe suppurative meningoencephalitis	Yes	1.ii.; 2b.i.; 3a.ii.; 4a.i.
7	Feline, Domestic shorthair	16	Hypertrophic cardiomyopathy	10/2/20	10/16/20	10/13/20	Hypertrophic cardiomyopathy, heart failure	Yes	1.ii.; 2b.i.; 3a.ii.; 4a.i.
8	Feline, Domestic shorthair	3	Urinary obstruction	1/1/21	1/4/21	1/2/21	Urinary Obstruction	Yes	1.i.; 2a.i.
9	Canine, Shepherd mix	9	Chronic airway disease	6/12/20	7/1/20	7/2/20	Chronic airway disease	Partial	1.ii.; 2b.i.; 3a.ii.; 4a.ii.
10	Feline, Domestic shorthair	4	Mild hypertrophic cardiomyopathy	12/10/20	12/15/20	12/15/20	SARS-CoV-2	Yes	1.ii.; 2b.ii.; 3b.ii.; 4b.ii.

\* Algorithm interpretation and Conclusions are based on a standardized algorithm that uses clinical presentation, co-morbidities, presence of virus in critical organs, and histopathological changes in tissues attributable to SARS-CoV-2 to determine whether SARS-CoV-2 infection was an incidental finding, a contributing factor, or the primary reason for an animal's death or euthanasia. This algorithm is presented in Figure 1

## Figures



**Figure 1**  
 Algorithm to determine the contribution of SARS-CoV-2 in animal death. \*Severe co-morbidities are likely to have resulted in animal death or euthanasia; \*\*Significant co-morbidities could contribute to the death of the animal but are unlikely to result in death; †Critical organs: heart, lungs, brain.

### Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SevereOutcomesSupplementalMaterialsResearchSquare.docx](#)