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Clinical and epidemiologic features of SARS-CoV-2 in dogs and cats compiled through national surveillance in the United States

Amanda Y. Liew, MPH[1*]; Ann Carpenter, DVM, MPH[1]; Taylor A. Moore, MPH[1]; Ryan M. Wallace, DVM, MPH[1]; Sarah A. Hamer, PhD, DVM, DACVPM[2]; Gabriel L. Hamer, PhD[3]; Rebecca S. B. Fischer, PhD, MPH, DTMH[4]; Italo B. Zecca, MPH, PhD[1,2]; Edward Davila, MPH[2]; Lisa D. Auckland, BS[2]; Jane A. Rooney, DVM[5]; Mary Lea Killian, MS[6]; Rachel M. Tell, DVM, PhD[6]; Steven I. Rekant, DVM, MPH, DACVPM[7]; Sierra D. Burrell, DVM, MPH[7]; Ria R. Ghai, PhD[1]; Casey Barton Behravesh, MS, DVM, DrPH, DACVPM[1]; and the Companion Animals Working Group

[1]CDC, Atlanta, GA
[2]Department of Veterinary Integrative Biosciences, Texas A&M University, College Station, TX
[3]Department of Entomology, Texas A&M University, College Station, TX
[4]School of Public Health, Texas A&M University College Station, TX
[5]Veterinary Services, APHIS, USDA, Fort Collins, CO
[6]National Veterinary Services Laboratories, APHIS, USDA, Ames, IA
[7]Veterinary Services, APHIS, USDA, Riverdale, MD

*Corresponding author: Amanda Liew (pnx6@cdc.gov)

The Companion Animals Working Group members are listed in the Acknowledgments at the end of this article.

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OBJECTIVE
To characterize clinical and epidemiologic features of SARS-CoV-2 in companion animals detected through both passive and active surveillance in the US.

ANIMALS
204 companion animals (109 cats, 95 dogs) across 33 states with confirmed SARS-CoV-2 infections between March 2020 and December 2021.

PROCEDURES
Public health officials, animal health officials, and academic researchers investigating zoonotic SARS-CoV-2 transmission events reported clinical, laboratory, and epidemiologic information through a standardized One Health surveillance process developed by the CDC and partners.

RESULTS
Among dogs and cats identified through passive surveillance, 94% (n = 87) had reported exposure to a person with COVID-19 before infection. Clinical signs of illness were present in 74% of pets identified through passive surveillance and 27% of pets identified through active surveillance. Duration of illness in pets averaged 15 days in cats and 12 days in dogs. The average time between human and pet onset of illness was 10 days. Viral nucleic acid was first detected at 3 days after exposure in both cats and dogs. Antibodies were detected starting 5 days after exposure, and titers were highest at 9 days in cats and 14 days in dogs.

CLINICAL RELEVANCE
Results of the present study supported that cats and dogs primarily become infected with SARS-CoV-2 following exposure to a person with COVID-19, most often their owners. Case investigation and surveillance that include both people and animals are necessary to understand transmission dynamics and viral evolution of zoonotic diseases like SARS-CoV-2.

Pet ownership provides many documented positive impacts, including improvements to mental health.[1,2] In the US, a 2021–2022 survey[3] reported that approximately 70% of households, or 90.5 million households, owned at least 1 pet, with around 23 million US households acquiring a pet during the first year of the COVID-19 pandemic (March 2020 through May 2021).[4] Owners and their pets commonly have close relationships, often eating, sleeping, snuggling, and recreating together.[5] While these close interactions have many benefits, they also pose a risk for zoonotic disease transmission. However, the extent of surveillance efforts to detect zoonotic disease transmission in companion animals, including SARS-CoV-2, is limited at both the national and global level.

Similar to some other coronaviruses, it is now evident that SARS-CoV-2 has a broad mammalian host range.[6] As of August 31, 2022, 36 countries have reported SARS-CoV-2 infections in species from 14 mammalian families to the World Organisation for Animal Health (WOAH).[7] Susceptible animals can be categorized into 4 groups by the nature of their interaction with people: companion animals, farmed animals (including mink[8] and cervids[9]), free-ranging wildlife,[10–12] and exotic animals (including big cats and nonhuman primates) in zoos, sanctuaries, and aquaria.[13] Companion animals are the second-most commonly reported animal group to be infected with SARS-CoV-2 after farmed mink,[8] composing 60% (n = 399 [205 cats, 191 dogs, 11 hamsters, and 3 ferrets]) of all animals reported globally to the WOAH between February 29, 2020, and December 31, 2021.[14]

In the present report, we used the largest compilation of zoonotic SARS-CoV-2 surveillance data available globally to synthesize the epidemiologic and clinical features of SARS-CoV-2 in companion animals, specifically dogs and cats, residing in the US.

Materials and Methods

Identifying companion animals confirmed positive for SARS-CoV-2

In the US, animal cases of SARS-CoV-2 are identified by passive or active surveillance. Through passive surveillance, case identification is typically initiated when owners bring animals to veterinary clinics or hospitals, and samples are submitted to a variety of veterinary diagnostic laboratories (governmental, university, and private) for SARS-CoV-2 testing. Through active surveillance, animals with a known SARS-CoV-2 exposure or clinical signs compatible with SARS-CoV-2 infection are actively sought out by health officials or researchers. These include collaborative One Health investigations of SARS-CoV-2 transmission among animals and people in households, animal shelters, animal rescues, animal rehabilitation centers, zoos, or veterinary clinics.[15–17] Regardless of whether animal cases are detected through passive or active surveillance, samples are first tested at governmental, university, or private veterinary diagnostic laboratories, many of which are members of the USDA's National Animal Health Laboratory Network. Test results from presumptive positive cases are shared with state and federal One Health partners, including public health and animal health officials,[18] and under most circumstances, these samples are forwarded to the USDA National Veterinary Services Laboratories (USDA-NVSL) to undergo confirmatory testing for SARS-CoV-2. For all analyses included in this manuscript, diagnostic testing results are used from the USDA-NVSL, whose methods have been previously described.[11,16] Animals confirmed positive for SARS-CoV-2 are reported by the USDA to the WOAH.[14]

According to the US case definition,[19] an animal is confirmed positive for SARS-CoV-2 at the USDA-NVSL if (1) SARS-CoV-2 sequence is generated either directly from suspect or presumptive positive animal samples or indirectly from a viral isolate recovered from that animal or (2) if serum from a suspect or presumptive positive animal demonstrates the presence of SARS-CoV-2–neutralizing antibody. Until March 2021, samples from every presumptive positive animal were requested to undergo confirmatory testing at the USDA-NVSL. After March 2021, confirmatory testing expectations changed for dogs and cats to include only the first dog and cat per state, territory, or tribal nation. To monitor viral changes, the USDA-NVSL continues to request submission of any dog and cat samples that (1) are strong sequencing candidates with SARS-CoV-2 real-time reverse transcription PCR (RT-PCR) cycle threshold (Ct) values < 30, (2) are associated with unusual morbidity and mortality events, or (3) are suspected or known to be infected with variants (eg, Alpha, Delta, Omicron).[18]

Our data set is composed of companion animals that met the US confirmed positive case definition from April 2020 through December 2021; these animals are also reported on the USDA's public dashboard.[20]

Data reporting

Early in the pandemic, CDC experts developed a One Health toolkit and standardized data collection forms for public and animal health officials to jointly guide epidemiologic investigations of animals suspected with SARS-CoV-2.[21] An electronic data reporting form was subsequently created in the CDC's online secure COVID-19 surveillance database, HHS Protect,[22] in which state health officials, including state public health veterinarians and state animal health officials, can provide standard information on animal cases of any species to CDC. The One Health Case Investigation Form for Animals with SARS-CoV-2[21] gathers information on animal signalment (species, age, sex), clinical signs, comorbidities, samples collected, and diagnostic results (including RT-PCR, sequencing, and virus neutralization [VN] or ELISA and the results of respiratory panels, if available). This form is also used to collect voluntarily reported information, often provided by the veterinarian or owner, including symptom onset dates, date of positive COVID-19 tests, and type and frequency of interactions with pets (eg, feeding, walking, playing, sharing same bed, or administering medications).

Data analyses

Data for this project were shared with the CDC by One Health partners and exported from HHS Protect case reports.[22] Data cleaning, visualization, and analytics occurred using statistical[23] and spreadsheet[24] software.

Clinical signs

We divided clinical signs into 3 categories based on body systems affected: respiratory (coughing, difficulty breathing or shortness of breath, sneezing, nasal discharge, ocular discharge), gastrointestinal (vomiting, diarrhea), and nonspecific (lethargy, inappetence, fever). Clinical signs were described in 4 subsets: (1) clinical versus subclinical among all

confirmed positive companion animals, (2) clinical versus subclinical based on surveillance detection method (active or passive surveillance), (3) detailed clinical signs among companion animals evaluated for illness, and (4) detailed clinical presentation among companion animals presenting with clinical signs by species.

Multipet households

In some instances, more than one companion animal was known to live in a household. To assess the likelihood that another animal in the household would become infected following the first, we calculated conditional probability, subset to only animals detected through passive surveillance (where an index pet could be identified). Conditional probabilities were calculated based on whether the index pet was a cat, dog, or either and whether the secondary animal was a cat, dog, or either.

Diagnostic testing

To understand timeline of infection and immune response of companion animals infected with SARS-CoV-2, we assessed Ct values (the number of cycles necessary for viral nucleic acid detection, with lower values indicating higher viral load) and VN titers (a measure of neutralizing antibody levels, indicating immune response) after an animal was exposed to a person with COVID-19. Sampling days were calculated as the number of days between a person's symptom onset or date of positive SARS-CoV-2 test and the animal's sample collection date. In animals with clinical signs, the length of observable illness was defined as the number of days between onset and resolution of clinical signs. While extremely rare, a small number of animals died while positive for SARS-CoV-2 (documented by Carpenter et al[25]). These animals were excluded from analyses of clinical signs but included in others where clinical signs were not the focus of evaluation. In analyses or visualizations that used Ct values, the lowest Ct value obtained from respiratory swabs (nasal and oral) collected on the same day was used. Nonrespiratory samples such as fecal and rectal samples were excluded since the viral load in these sample types is commonly low (ie, higher average Ct values) compared with that in respiratory samples.[26] The diagnostic efficacy of conjunctival swabs has not been evaluated. Since they were also infrequently collected, they were excluded from analyses. Fur swabs were also omitted from analyses since they are used as indicators of environmental contamination and not infection.

SARS-CoV-2 RT-PCR results, measured by Ct, and SARS-CoV-2 VN titers were compared with the presumed date of exposure, measured as the reported date of human symptom onset or positive human test. The lowest Ct values among respiratory swabs (oral and nasal) and geometric mean titer were calculated in 2-day intervals with 95% CIs. Average Ct values and log-transformed geometric mean virus-neutralizing antibody titers were calculated for confirmed animals, by species. Analysis was conducted for all observations, as well as a stratified analysis by species. To account for the inherent rise and fall of viral nucleic acid and neutralizing antibody, a polynomial function was applied to detect trends in Ct values and VN titer over time since presumed exposure. As early sampling in the first several days after exposure was rarely conducted, fixed axis points were applied to the regression model to reflect a Ct of 40 (no viral nucleic acid present) and VN of 0 on the day of likely exposure (day 0). Two animals with Ct values < 38 on the day of presumed exposure (day 0) were excluded from analysis, as it is not biologically plausible to have measurable infection or immunity this early after exposure. It is likely that the date of presumed exposure occurred earlier than what was reflected in the epidemiologic investigation for these 2 animals.

Variant analysis was conducted using whole-genome sequencing results from the USDA-NVSL. In late 2020, SARS-CoV-2 variants were identified and classified by the CDC based on their impacts to human health, diagnostics, therapeutics, and vaccines.[27] In this study, strains sequenced prior to the identification of the first variants were classified as early circulating strains.

Epidemiologic links

In analyses or visualizations that described the association between human SARS-CoV-2 infection and animal infection, a person's symptom onset date was assumed to represent the most likely date of exposure in the animal. In instances where this date was not available, the date the person first tested positive for COVID-19 was used.

To assess whether population increases in COVID-19 in people might cause subsequent increases in companion animal cases, a time series analysis using a cross-correlation function was performed to determine whether there was a relationship between national human COVID-19 case reporting data and SARS-CoV-2 cases in companion animals. Daily national human COVID-19 case counts were downloaded from the CDC's COVID Data Tracker and aggregated into monthly counts from March 2020 to December 2021.[28] SARS-CoV-2 infections in cats and dogs were aggregated into monthly counts. Sample collection date, which was available for 161 of 204 (79%) animals, was used as a proxy for date of infection. The cross-correlation time series analysis was restricted to 1 year, March 2020 to March 2021, since all presumptive positive companion animal cases were forwarded to the USDA-NVSL for confirmatory testing during this time.

Results

Overview

From March 2020 to December 2021, 345 animals from 33 states in the US were confirmed positive for SARS-CoV-2 **(Figure 1; Supplementary Figure S1)**. Of these, 204 (59%) were companion animals, including 109 cats and 95 dogs **(Table 1;**

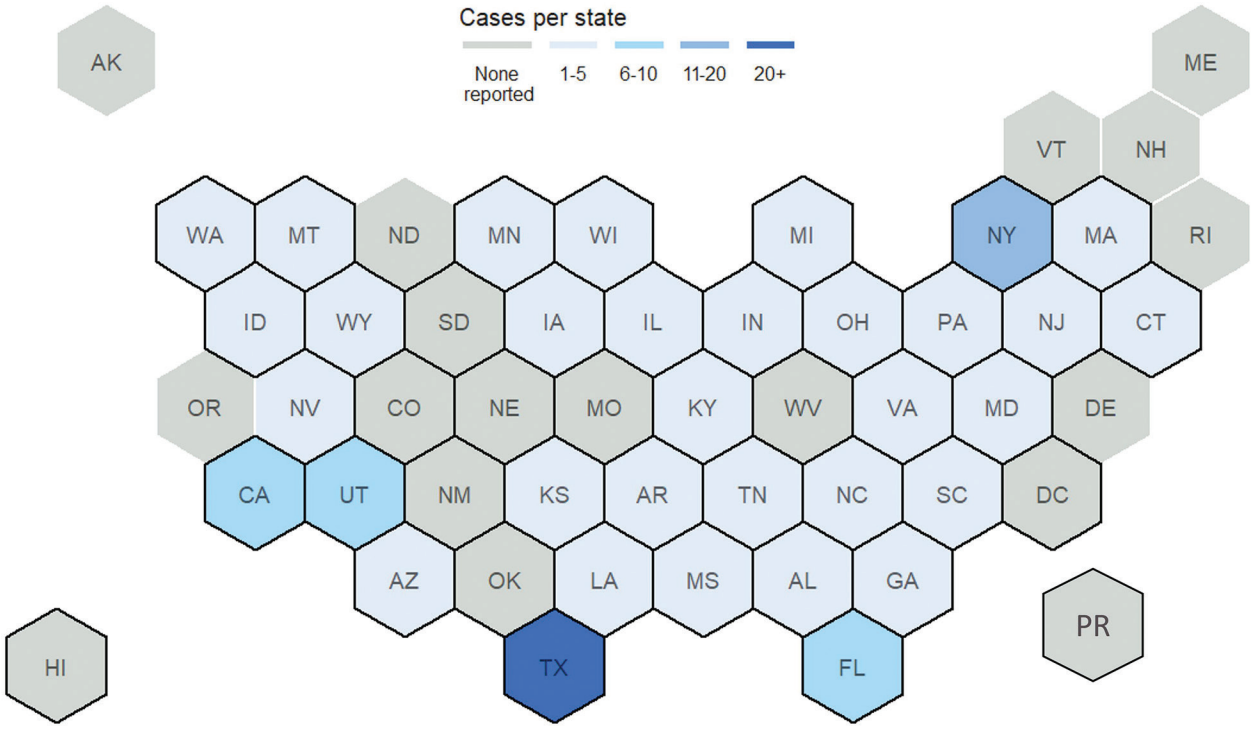

Figure 1—Distribution of positive animal cases reported by jurisdictions. States reporting any positive animal cases, including zoo and wildlife, are outlined in black, while states with positive companion animals are shaded in blue. States shaded gray without a black outline did not report any SARS-CoV-2–positive animal cases, while states shaded in gray with a black outline did not report companion animal cases but did report SARS-CoV-2–positive zoo and/or wildlife.

Table 1—Demographics of confirmed positive companion animals in the US from March 2020 through December 2021.

Variable	Cat	Dog
No.	109	95
Sex (No. [%])		
Female	23 (21.1)	18 (18.9)
Male	38 (34.9)	26 (27.4)
Unknown	48 (44.0)	51 (53.7)
Age (y; mean [SD])	6.64 (4.69)	6.89 (4.19)

Supplementary Table S1). SARS-CoV-2 was also detected by RT-PCR in 1 ferret; this animal was omitted from further analyses due to low sample size. In companion animal cases detected through passive surveillance, 94% were initially exposed to a person with COVID-19. In the remaining 6% of cases, the source of SARS-CoV-2 exposure was unknown (eg, circumstances such as an animal tested positive upon arrival at a shelter or owners declined investigation).

Clinical signs

Overall, 48% (n = 97) of companion animals displayed clinical signs consistent with SARS-CoV-2 infection, while 52% (107) had no reported clinical signs at the time of sampling. This varied significantly by surveillance method ($\chi^2[1] = 41.07$; $P < .0001$); 72% (n = 67) of animals identified through passive surveillance exhibited clinical signs, while only 27% (30) of animals identified through active surveillance exhibited clinical signs.

Respiratory signs (n = 81 [84%]) were most frequently reported among animals with clinical signs, followed by nonspecific (53 [55%]) and gastrointestinal (16 [16%]) signs. Clinical presentation also varied by species **(Figure 2)**; 50% (n = 55) of cats and 44% (42) of dogs showed clinical signs, although this variation was not statistically significant ($\chi^2[1] = 3.42$; $P = .065$). Of the animals with clinical signs, sneezing (21%) and lethargy (16%) were the most common in cats, whereas lethargy (20%) and cough (16%) were most common in dogs.

Multipet households

Thirty-six households had more than 1 cat or dog. There was a 25% (Wilson CI, 14% to 41%) likelihood that if 1 cat or dog was infected in the household, a second cat or dog would also test positive for SARS-CoV-2 (data not shown). Probability was higher of a second cat or dog testing positive if the index pet was a cat (30%; Wilson CI, 16% to 51%), and probability was lower, although not significant, if the index pet was a dog (15%; Wilson CI, 4% to 42%).

Diagnostic testing

Of the 204 confirmed positive companion animals, 91 (45%) tested positive by VN only, 67 (33%) tested positive by RT-PCR only, and 46 (23%) tested positive by both RT-PCR and VN **(Supplementary Table S2)**.

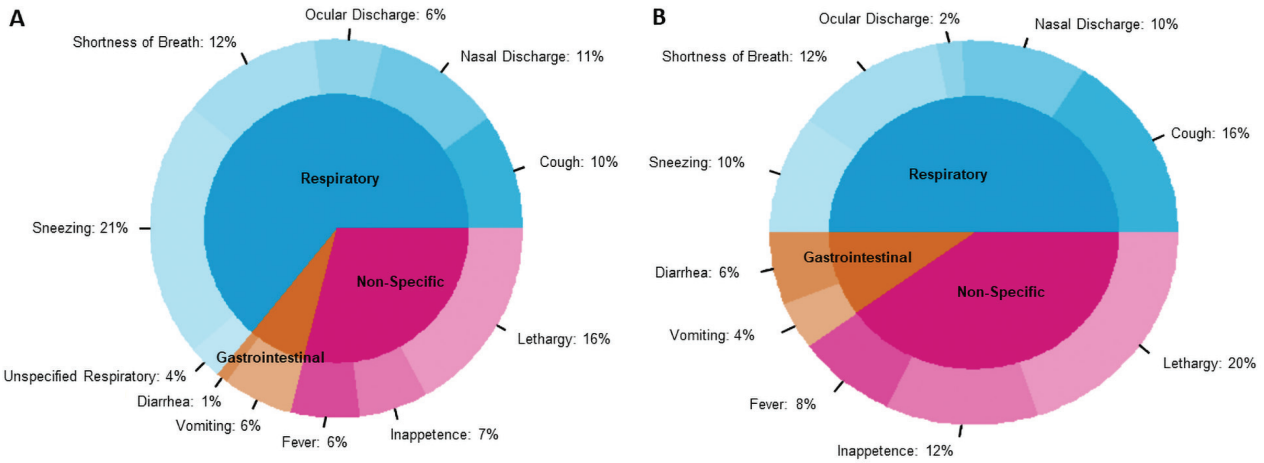

Figure 2—Clinical signs reported in cats (n = 55; A) and dogs (42; B). Of 97 animals with clinical signs, the proportion of each clinical sign being displayed is shown within each species. Since a given animal may display multiple clinical signs, percentages are calculated by number of signs displayed, not by individual animals.

The average Ct value from confirmatory RT-PCR was 28.6 for all confirmed positive companion animals with RT-PCR results (n = 69). VN titers (n = 107) ranged from 8 to 512, with a median titer of 64 (geometric mean titer of 1.8) for all confirmed positive companion animals. Titers from confirmed positive cats ranged from 32 to 512 with a median titer of 128 (geometric mean of 1.9), whereas results from dogs ranged from 8 to 128 with a median titer of 32 (geometric mean of 1.6). The highest titer of 512 was detected in a cat sampled 23 days after onset of symptoms in its owner.

Associations between SARS-CoV-2 nucleic acid detection and virus-neutralizing antibodies differed by species and were analyzed separately. Molecular detection was as early as 3 days after exposure for both cats and dogs **(Figure 3)**. Ct values for SARS-CoV-2 nucleic acid detection peaked at day 6 for cats (Ct = 27) and day 5 for dogs at (29). Detection occurred, on average, up to day 23 after most likely exposure in cats (range, 15 to 33 days) and up to 13 days in dogs (range, 9 to 16 days). In cats, virus-specific antibodies were first detected 5 days after nucleic acid detection

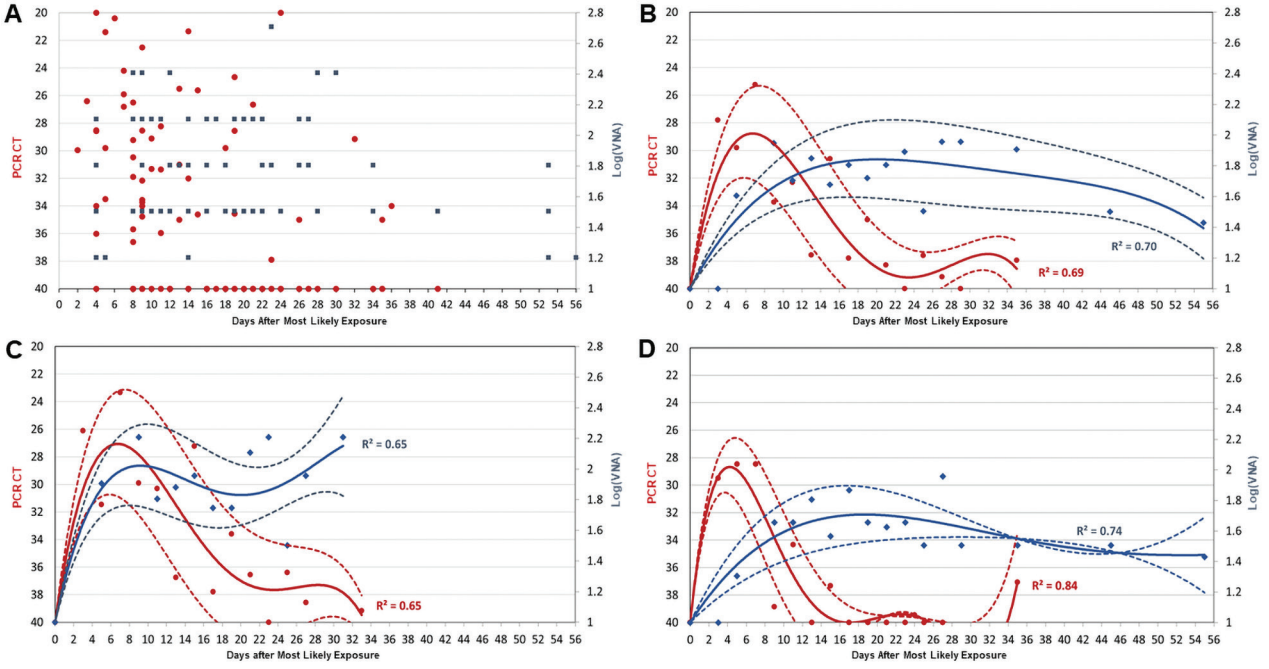

Figure 3—Trends in SARS-CoV-2 nucleic acid detection and virus-neutralizing antibodies in dogs and cats with confirmed infection, 2019 through 2021. Red lines and red circles represent cycle threshold values from the SARS-CoV-2 real-time quantitative PCR assay. Blue lines and blue squares represent virus-neutralizing antibody titers (VNA). A—All dogs and cats registered as confirmed with SARS-CoV-2 infection during the study period / Individual values represented for each animal. B—All dogs and cats / Average values represented over 2-day sampling frames with CIs (dotted lines). C—Only cats. D—Only dogs.

(5 days after presumed exposure) and peaked at a geometric titer of 2.1 on day 32 after exposure. For dogs, virus-specific antibodies were first measurable 3 days after nucleic acid detection (5 days after exposure) and peaked at a geometric titer of 1.7 at 18 days after exposure. Although sample size was limited at longer sampling periods, antibody titers gradually trended downwards, but appeared stable at a geometric titer of 1.5 through at least day 55 after exposure.

Whole genome sequencing was successful on samples from 70 (34%) animals (n = 41 cats and 29 dogs). Early circulating strains **(Supplementary Table S3)** and 4 variants were detected: Alpha (B.1.1.7),[29] Delta (B.1.617.2), Epsilon (B.1.429), and Iota (B.1.526). In animals with early circulating SARS-CoV-2 strains (n = 37), lethargy (48%) and shortness of breath (43%) were the most commonly reported (23; **Supplementary Table S4**). There were more clinically ill cats (n = 30 [73%]) than dogs (18 [62%]), but there was no significant difference in signs of illness between species ($\chi^2[1] = 0.94$; $P = .333$). Delta was the most common variant detected (n = 21).

Epidemiologic links

To estimate viral incubation period, the number of days between human symptom onset (or date of positive test) and onset of clinical signs in animals was calculated. Data for this analysis were restricted to animals with clinical signs and animals for which data were available to show that a person in the house had symptoms (n = 32; **Figure 4**). The median number of days between human symptom onset and onset of clinical signs in a companion animal was 10 days (interquartile range [IQR], 9.5 days; range, 0 to 24 days) in cats (n = 23) and 6 days (IQR, 8 days; range, 1 to 24 days) in dogs (9). We also assessed the length of active infection using clinical sign onset and resolution dates. According to data from confirmed RT-PCR–positive animals, excluding deceased animals, with both onset and resolution dates collected (n = 24), the median length of clinical infection was 10 days (IQR, 7.25 days; range, 3 to 36 days) in cats (n = 16) and 16.5 days (IQR, 10.75 days; range, 1 to 31 days) in dogs (8).

The likelihood of detecting an active infection by RT-PCR is largely dependent on the length of time between the animal's most likely exposure to SARS-CoV-2 and the sample collection date. The median delay from presumed exposure date to animal sampling for a positive RT-PCR result was 10 days (IQR, 9 days; range, 0 to 35 days) in cats (n = 35) and 6 days (IQR, 5.5 days; range, 0 to 24 days) in dogs (15; Figure 4).

We also investigated whether patterns in human case counts were predictive of companion animal case counts. Given the available data in the restricted timeframe, a time series analysis using a cross-correlation function determined that while there appeared to be an observable relationship between human and animal case counts, this relationship was not significant **(Figure 5)**.

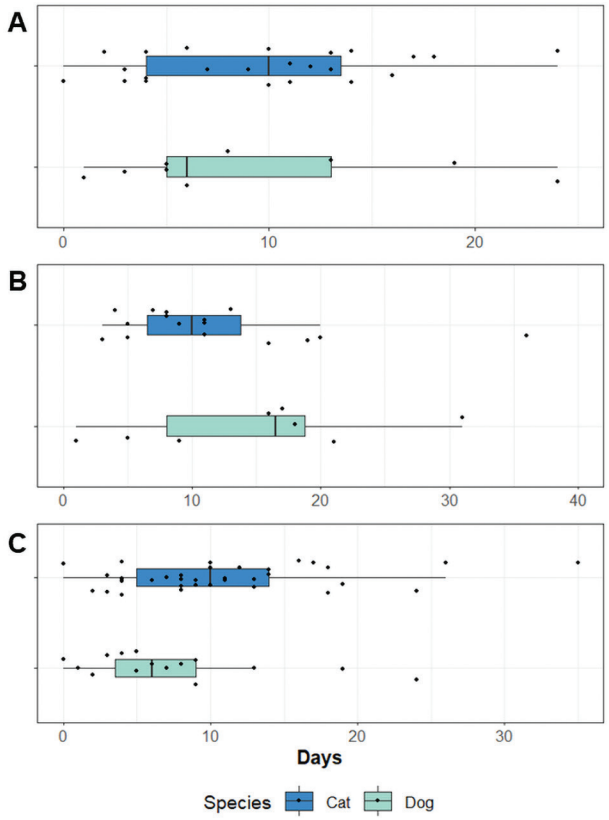

Figure 4—A—Timeline of days between human symptom onset and animal clinical sign onset. This analysis excludes subclinical animals. Jittering was used to better visualize distribution of the data and to prevent overlapping of values, with each point corresponding to an individual animal. B—Days between clinical sign onset and resolution in animals. This serves to characterize the length of active infection in affected animals. Deceased animals were excluded from this analysis. C—Days between human symptom onset and positive animal test. The animal test date referenced is the collection date of the sample that yielded a positive real-time reverse transcription PCR result. This includes both clinically affected and subclinical animals.

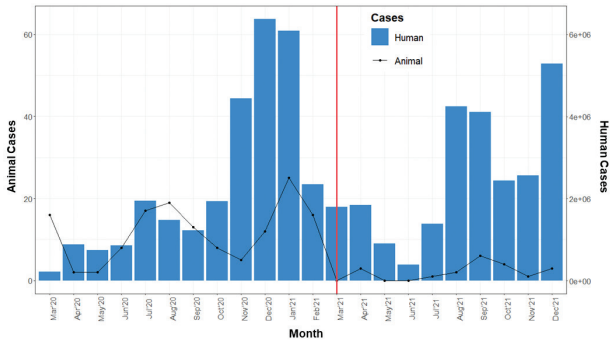

Figure 5—Time series of human COVID-19 monthly case count and animal infections of SARS-CoV-2. For animal cases, the date of sample collection was used. Effective March 2021, indicated by the red line, USDA expectations for confirmatory testing for companion animals were changed to include only the first domestic cat and dog in each state, territory, and tribal nation.

Discussion

This study is the first to summarize nationally compiled surveillance data on the epidemiologic and clinical characteristics of natural SARS-CoV-2 infection in companion animals. While there are publications describing SARS-CoV-2 in companion animals in many countries, including those in Europe[30–36] and Asia,[37,38] studies are often led by academic institutions conducting independent research; surveillance is not sustainable or systematic. In the US, data on SARS-CoV-2–positive animals is collected through systematic One Health investigations and is shared voluntarily through collaborations with local, state, and federal officials as well as academic public health and animal health officials.[15–17,25] Given that human COVID-19 case counts in the US have been equivalent to those of other countries, these robust surveillance efforts to detect SARS-CoV-2 in animals may partly explain why the majority (56%) of all companion animal cases reported globally are from the US.[14]

There are 3 transmission pathways that may be considered during epidemiologic investigation of zoonotic SARS-CoV-2 events: human to animal, animal to animal, and animal to human. Overall, our data showed that among SARS-CoV-2–infected companion animals detected through passive surveillance, 94% had known exposure to a person with COVID-19 prior to the animal's infection. This provided strong evidence that people, most often owners, are the source of infection for their pets. These results corroborated findings from other studies, including those where pet infection is more likely in households with a history of COVID-19.[30,39,40] This finding also supported guidance developed by federal One Health partners that includes recommendations that when people are sick or have a suspected COVID-19 infection, they should avoid contact with animals, just like they would with other people, and that they should wear a mask around both people and animals when ill with COVID-19.[41]

While the evidence for human-to-pet transmission is robust, less data are available to determine the likelihood and frequency of pet-to-pet or pet-to-person transmission within households. Our analysis of 36 households containing more than 1 pet indicated that any cat or dog in the household has a 25% probability of becoming infected with SARS-CoV-2 if there is a positive index pet. This probability was higher when cats were the index pet (30%) than when dogs were (15%), in line with experimental and challenge studies that suggest cats are more susceptible[42,43] and may be more infectious based on lower overall Ct values than dogs. While these data suggest pet-to-pet transmission may occur in households, we cannot determine whether subsequent pets in a multipet household were infected from a person or another animal. More One Health research to examine transmission dynamics among animals and among animals and people living in household environments is warranted.

To date, evidence of cats or dogs transmitting SARS-CoV-2 to people is limited, although detecting and accurately attributing transmission from an animal source is challenging against a background of significant human-to-human transmission. However, 1 recent case study suggests cat-to-human transmission as likely from an infected pet cat in Thailand,[44] while another identified imported hamsters for sale as the likely source of infection and onward spread among people in Hong Kong.[45]

With respect to clinical presentation in pets, 48% of all SARS-CoV-2–confirmed companion animal cases exhibited clinical signs. Respiratory signs, particularly sneezing and cough, were the most common among ill animals. The proportion of animals with clinical signs varied significantly by surveillance method. Active surveillance studies, which typically begin when a person with COVID-19 is identified, and where companion animal samples are sought irrespective of their health, are likely a more accurate estimate of companion animal infection prevalence nationally. Overall, only 27% of actively infected (evidenced by detection of viral nucleic acid) companion animals sampled through active surveillance showed clinical signs, emphasizing that subclinical animals should not be discounted when evaluating the role of animals in SARS-CoV-2 transmission.[46]

Our study also estimated thresholds of diagnostic detection in companion animals. Data from 142 companion animals (74 cats, 68 dogs) sampled after presumed exposure to a person with SARS-CoV-2 suggests that viral nucleic acid detection by RT-PCR occurs shortly after presumed exposure, typically < 5 days. Our data suggested that the ideal sampling window to detect viral nucleic acid is 3 to 17 days after exposure for cats and 3 to 10 days after exposure for dogs (Figure 4). We also discovered that virus-specific neutralizing antibody is rapidly produced. Rapid and sustained titers of neutralizing antibody after infection may have contributed to the mild nature of disease observed in the majority of animals in this study (see Carpenter et al,[25] Carvallo et al,[47] and Rotstein et al[48] for descriptions of companion animal mortalities that occurred while pets were positive for SARS-CoV-2). These findings may be useful to inform veterinary and public health recommendations for clinical testing and case management in companion animals and may be a starting point to infer similar guidance for other animals under human care where robust data do not exist, such as those in zoos, sanctuaries, aquaria, and rehabilitation facilities.

Finally, samples from 34% of companion animals included in our data were successfully characterized by whole genome sequencing. These sequences were used to identify variants and their corresponding clinical presentation (Supplementary Table S4). Among this subset, early circulating strains and 4 variants were detected: each corresponded temporally with variants circulating in the human populations in the same geographic area at the time. Processes to continue to generate and analyze sequence information from animal populations are essential to ensure that novel mutations, strains, and variants arising from animal populations, including companion animals, are detected expediently, ideally before detrimental impacts to public health can be recognized.[49]

Some limitations exist regarding the nature of data collection and the analyses presented in this manuscript. First, no federal agency is currently mandated to oversee companion animal surveillance or response, including for emerging zoonotic diseases. Reporting for companion animal zoonoses to public or animal health officials may also be jurisdiction or disease specific. Given that surveillance varies by jurisdiction, the approach taken by One Health investigations and reporting are likely to have varied. Ongoing efforts to improve surveillance, including enhancing coordination and data sharing among One Health sectors and supporting data modernization initiatives, are underway.[50] Second, since there is no standardized diagnostic method or sample validation criteria for SARS-CoV-2 in animals in the US, we opted to include only companion animals that were confirmed positive at the USDA-NVSL to ensure consistency and comparability in diagnostic results. In doing so, however, we limited our sample size and perhaps skewed results toward animals that met standards of confirmation. Third, our analysis based on a human source of exposure does not account for households where multiple people may have been the source of pet infections, as symptom onset and positive test dates were recorded for only the first identified person with COVID-19 in each household. The date of animal exposure should therefore be considered an estimation. Fourth, epidemiologic information, including human symptom onset or animal clinical sign onset dates, was reported by veterinarians and owners and is therefore subject to the variability associated with self-reporting. Fifth, animals may have presented to veterinary clinics with clinical signs not caused by SARS-CoV-2. Without additional testing data to rule out other diseases, we cannot entirely attribute clinical signs to SARS-CoV-2 infection. Finally, our results and interpretations are based on early circulating strains of SARS-CoV-2 and the 4 variants, including Delta, identified in companion animals before the end of 2021. This data set does not extend into 2022, when Omicron became the most prevalent variant in the US; conclusions about companion animal susceptibility, duration of infection, and transmissibility may be altered for animals infected with Omicron due to the virus's high number of mutations and are not addressed here. Future studies that implement a standardized approach to sample collection among all members of a household (both human and animal) and sample longitudinally through time may provide needed clarity to understand the role companion animals play in SARS-CoV-2 transmission at the human–companion animal interface.

Given that SARS-CoV-2 infections in animals are not currently nationally notifiable in the US, it is possible that unreported animal cases were missed within the timeframe of the data included in this manuscript. This is corroborated by published research, which also suggests that current surveillance may be vastly underestimating the true burden of SARS-CoV-2 in animals.[15–17,36] Without continued One Health collaboration across sectors to pursue more extensive surveillance (both active and passive), many SARS-CoV-2 infections in companion animals will remain undetected.

Despite the known susceptibility of companion animals to SARS-CoV-2, testing efforts and disease reporting of pet cases of SARS-CoV-2 infection have been limited in the US. Lack of mandatory reporting of companion animal cases of SARS-CoV-2 infection has continued to be a challenge throughout the COVID-19 pandemic. Relying on voluntary reporting of a novel, emerging zoonotic disease with unknown transmissibility and disease in animals is a hurdle for understanding the clinical and epidemiologic features of a rapidly spreading zoonosis. This is especially apparent with companion animals, whose oversight falls in a government jurisdictional gap, and where structures and systems to detect, monitor, and respond to companion animal zoonoses are typically not a standard component of public health or animal health programs. The present report provides support to the idea that systematic surveillance in animal populations can be established, sustained, and beneficial in a global public health emergency. In the instance of SARS-CoV-2, strong collaborations between public health and animal health sectors at the local, state, and federal level were able to circumvent some of these issues. However, formalized One Health collaboration mechanisms that institutionalize joint investigation and coordinated surveillance are necessary to best protect human and animal health and to most efficiently respond to future emerging zoonotic disease threats.

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All data are part of national surveillance and available on the USDA's public-facing dashboard (https://publicdashboards.dl.usda.gov/t/MRP_PUB/views/VS_CrossCommodity_SARS-CoV2Cases/OverviewofCases?:embed_code_version=3&:embed=y&:isGuestRedirectFromVizportal=y&:loadOrderID=0&:display_spinner=no&:display_count=n&:showVizHome=n&:origin=viz_share_link).

Members of the Companion Animals Working Group: Heather Venkat, DVM, MPH (Arizona Department of Health Services, Phoenix, AZ); Laura Rothfeldt, DVM (Arkansas Department of Health, Little Rock, AR); Rebecca Campagna, DVM, MPH, DACVPM (California Department of Public Health, Sacramento, CA); Curtis Fritz, DVM, MVPM, PhD, DACVPM (California Department of Public Health, Sacramento, CA); Jane Lewis, DVM, MS, DACVPM (Connecticut Department of Agriculture, Hartford, CT); Michael Short, DVM (Florida Department of Agriculture and Consumer Services, Tallahassee, FL); Danielle Stanek, DVM (Florida Department of Health, Tallahassee, FL); Amanda Feldpausch, DVM, MPH (Georgia Department of Public Health, Atlanta, GA); Marcus Webster, DVM, CertAqV (Georgia Department of Agriculture, Atlanta, GA); Kelly Giesbrecht, DVM, MPH (Kentucky Department for Public Health, Frankfort, KY); Joni Scheftel, DVM, MPH

(Minnesota Department of Health, Saint Paul, MN); Darby McDermott, DVM, MPH (New Jersey Department of Health, Trenton, NJ); Manoel Tamassia, DVM, PhD, DACT (New Jersey Department of Agriculture, Trenton, NJ); Patricia A. Zinna, DVM, MS (New Jersey Department of Health, Trenton, NJ); Betsy Schroeder, DVM, PhD, MPH, DACVPM (Pennsylvania Department of Health, Harrisburg, PA); Rachel Radcliffe, DVM, MPH (South Carolina Department of Health and Environmental Control, Columbia, SC); Samantha Beaty, DVM (Tennessee Department of Agriculture, Nashville, TN); John R. Dunn, DVM, PhD (Tennessee Department of Health, Nashville, TN); Yao Akpalu, PhD, MPH (Brazos County Health Department, Bryan, TX); Alexandra Colemere, MA, MPH (Texas Department of State Health Services, Austin, TX); Paul Grunenwald, DVM, MS, DACVPM (Texas Department of State Health Services, Austin, TX); William A. Lanier, DVM, MPH (Utah Department of Health and Human Services, Salt Lake City, UT); Hannah Rettler, MPH (Utah Department of Health and Human Services, Salt Lake City, UT); Charles C. Broaddus, DVM, PhD, DACT (Virginia Department of Agriculture and Consumer Services, Richmond, VA); Julia Murphy, DVM, MS, DACVPM (Virginia Department of Health, Richmond, VA); Beth Lipton, DVM, MPH (Public Health—Seattle and King County, Seattle, WA); Rachel Busselman, BS (Texas A&M University, College Station, TX); Ailam Lim, PhD (Wisconsin Veterinary Diagnostic Laboratory, Madison, WI); Julianne Meisner, BVMS, PhD (University of Washington, Seattle, WA); Michael J. Neault, DVM (Clemson University Livestock Poultry Health, Columbia, SC); Peter M. Rabinowitz, MD, MPH (University of Washington, Seattle, WA); Vickie Ramirez, MA (University of Washington, Seattle, WA); Christopher M. Roundy, PhD, MSPH (Texas A&M University, College Station, TX); Wendy Tang, PhD (Texas A&M University, College Station, TX); Grace W. Goryoka, MPH (CDC, Atlanta, GA); Melinda Jenkins-Moore, BS (National Veterinary Services Laboratories, APHIS, USDA, Ames, IA); Natalie M. Wendling, DVM, MPH, DACVPM (CDC, Atlanta, GA).

References

1. Clements H, Valentin S, Jenkins N, et al. Companion animal type and level of engagement matter: a mixed-methods study examining links between companion animal guardianship, loneliness and well-being during the COVID-19 pandemic. *Animals (Basel)*. 2021;11(8):11. doi:10.3390/ani11082349
2. Martin F, Bachert KE, Snow L, Tu HW, Belahbib J, Lyn SA. Depression, anxiety, and happiness in dog owners and potential dog owners during the COVID-19 pandemic in the United States. *PLoS One*. 2021;16(12):e0260676. doi:10.1371/journal.pone.0260676
3. Pet industry market size, trends & ownership statistics. American Pet Products Association. Accessed March 24, 2022. https://www.americanpetproducts.org/press_industrytrends.asp
4. New ASPCA survey shows overwhelming majority of dogs and cats acquired during the pandemic are still in their homes. American Society for the Prevention of Cruelty to Animals. Accessed March 24, 2022. https://www.aspca.org/about-us/press-releases/new-aspca-survey-shows-overwhelming-majority-dogs-and-cats-acquired-during
5. Chomel BB, Sun B. Zoonoses in the bedroom. *Emerg Infect Dis*. 2011;17(2):167–172. doi:10.3201/eid1702.101070
6. Ghai RR, Carpenter A, Liew AY, et al. Animal reservoirs and hosts for emerging alphacoronaviruses and betacoronaviruses. *Emerg Infect Dis*. 2021;27(4):1015–1022. doi:10.3201/eid2704.203945
7. World Organisation for Animal Health. *SARS-CoV-2 in Animals – Situation Report 16*. World Organisation for Animal Health; 2022.
8. Pomorska-Mól M, Włodarek J, Gogulski M, Rybska M. Review: SARS-CoV-2 infection in farmed minks - an overview of current knowledge on occurrence, disease and epidemiology. *Animal*. 2021;15(7):100272. doi:10.1016/j.animal.2021.100272
9. Roundy CM, Nunez CM, Thomas LF, et al. High Seroprevalence of SARS-CoV-2 in white-tailed deer (*Odocoileus virginianus*) at one of three captive cervid facilities in Texas. *Microbiol Spectr*. 2022;10(2):e0057622. doi:10.1128/spectrum.00576-22
10. Kuchipudi SV, Surendran-Nair M, Ruden RM, et al. Multiple spillovers from humans and onward transmission of SARS-CoV-2 in white-tailed deer. *Proc Natl Acad Sci USA*. 2022;119(6):e2121644119. doi:10.1073/pnas.2121644119
11. Hale VL, Dennis PM, McBride DS, et al. SARS-CoV-2 infection in free-ranging white-tailed deer. *Nature*. 2022;602(7897):481–486. doi:10.1038/s41586-021-04353-x
12. Chandler JC, Bevins SN, Ellis JW, et al. SARS-CoV-2 exposure in wild white-tailed deer (*Odocoileus virginianus*). *Proc Natl Acad Sci U S A*. 2021;118(47):e2114828118. doi:10.1073/pnas.2114828118
13. Allender MC, Adkesson MJ, Langan JN, et al. Multi-species outbreak of SARS-CoV-2 Delta variant in a zoological institution, with the detection in two new families of carnivores. *Transbound Emerg Dis*. 2022;69(5):e3060–e3075. doi:10.1111/tbed.14662
14. World Animal Health Information System animal disease events. World Organisation for Animal Health. Accessed August 31, 2022. https://wahis.woah.org/#/home
15. Goryoka GW, Cossaboom CM, Gharpure R, et al. One health investigation of SARS-CoV-2 infection and seropositivity among pets in households with confirmed human COVID-19 cases—Utah and Wisconsin, 2020. *Viruses*. 2021;13(9):13. doi:10.3390/v13091813
16. Hamer SA, Pauvolid-Corrêa A, Zecca IB, et al. SARS-CoV-2 infections and viral isolations among serially tested cats and dogs in households with infected owners in Texas, USA. *Viruses*. 2021;13(5):938. doi:10.3390/v13050938
17. Dileepan M, Di D, Huang Q, et al. Seroprevalence of SARS-CoV-2 (COVID-19) exposure in pet cats and dogs in Minnesota, USA. *Virulence*. 2021;12(1):1597–1609. doi:10.1080/21505594.2021.1936433
18. APHIS Veterinary Services. SARS-CoV-2 virus in animals: testing strategies and reporting expectations. March 2021. Accessed March 24, 2022. https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-testing-strategies.pdf
19. APHIS Veterinary Services. *SARS-CoV-2. Case Definition – June 11*. USDA; 2021.
20. Confirmed cases of SARS-CoV-2 in animals in the United States. APHIS Veterinary Services. Accessed August 31, 2022. https://www.aphis.usda.gov/aphis/dashboards/tableau/sars-dashboard
21. One Health toolkit for health officials managing companion animals with SARS-CoV-2. CDC. March 23, 2021. Accessed March 23, 2022. https://www.cdc.gov/coronavirus/2019-ncov/animals/toolkit.html
22. HHS Protect public data hub. US Department of Health and Human Services. Accessed August 31, 2022. https://public-data-hub-dhhs.hub.arcgis.com/
23. R Core Team. *R: A Language and Environment for Statistical Computing.* R Foundation for Statistical Computing; 2020.
24. *Excel*. Microsoft Corp; 2021.
25. Carpenter A, Ghai RR, Gary J, et al. Determining the role of natural SARS-CoV-2 infection in the death of domestic pets: 10 cases (2020–2021). *J Am Vet Med Assoc*. 2021;259(9):1032–1039. doi:10.2460/javma.259.9.1032
26. Pedersen RM, Tornby DS, Bang LL, et al. Rectally shed SARS-CoV-2 in COVID-19 inpatients is consistently lower than respiratory shedding and lacks infectivity. *Clin Microbiol Infect*. 2022;28(2):304.e1–304.e3. doi:10.1016/j.cmi.2021.10.023

27. SARS-CoV-2 variant classifications and definitions. CDC. Accessed March 24, 2022. https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html
28. Trends in number of COVID-19 cases and deaths in the US reported to CDC, by state/territory. CDC. Accessed March 24, 2022. https://covid.cdc.gov/covid-data-tracker/#trends_dailycases
29. Hamer SA, Ghai RR, Zecca IB, et al. SARS-CoV-2 B.1.1.7 variant of concern detected in a pet dog and cat after exposure to a person with COVID-19, USA. *Transbound Emerg Dis*. 2022;69(3):1656–1658. doi:10.1111/tbed.14122
30. Patterson EI, Elia G, Grassi A, et al. Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy. *Nat Commun*. 2020;11(1):6231. doi:10.1038/s41467-020-20097-0
31. Michelitsch A, Hoffmann D, Wernike K, Beer M. Occurrence of antibodies against SARS-CoV-2 in the domestic cat population of Germany. *Vaccines (Basel)*. 2020;8(4):8. doi:10.3390/vaccines8040772
32. Stevanovic V, Tabain I, Vilibic-Cavlek T, et al. The emergence of SARS-CoV-2 within the dog population in Croatia: host factors and clinical outcome. *Viruses*. 2021;13(8):13. doi:10.3390/v13081430
33. Smith SL, Anderson ER, Cansado-Utrilla C, et al. SARS-CoV-2 neutralising antibodies in dogs and cats in the United Kingdom. *Curr Res Virol Sci*. 2021;2:100011. doi:10.1016/j.crviro.2021.100011
34. Fritz M, Rosolen B, Krafft E, et al. High prevalence of SARS-CoV-2 antibodies in pets from COVID-19+ households. *One Health*. 2021;11:100192. doi:10.1016/j.onehlt.2020.100192
35. Schulz C, Martina B, Mirolo M, et al. SARS-CoV-2-specific antibodies in domestic cats during first COVID-19 wave, Europe. *Emerg Infect Dis*. 2021;27(12):3115–3118. doi:10.3201/eid2712.211252
36. Barroso R, Vieira-Pires A, Antunes A, Fidalgo-Carvalho I. Susceptibility of pets to SARS-CoV-2 infection: lessons from a seroepidemiologic survey of cats and dogs in Portugal. *Microorganisms*. 2022;10(2):345. doi:10.3390/microorganisms10020345
37. Zhang Q, Zhang H, Gao J, et al. A serological survey of SARS-CoV-2 in cat in Wuhan. *Emerg Microbes Infect*. 2020;9(1):2013–2019. doi:10.1080/22221751.2020.1817796
38. Udom K, Jairak W, Chamsai E, et al. Serological survey of antibodies against SARS-CoV-2 in dogs and cats, Thailand. *Transbound Emerg Dis*. 2022;69(4):2140–2147. doi:10.1111/tbed.14208
39. Bonilla-Aldana DK, García-Barco A, Jimenez-Diaz SD, et al. SARS-CoV-2 natural infection in animals: a systematic review of studies and case reports and series. *Vet Q*. 2021;41(1):250–267. doi:10.1080/01652176.2021.1970280
40. Kannekens-Jager MM, de Rooij MMT, de Groot Y, et al. SARS-CoV-2 infection in dogs and cats is associated with contact to COVID-19-positive household members. *Transbound Emerg Dis*. Published online September 26, 2022. doi:10.1111/tbed.14713
41. Healthy pets, healthy people. CDC. Accessed March 24, 2022. https://www.cdc.gov/healthypets/index.html
42. Shi J, Wen Z, Zhong G, et al. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. *Science*. 2020;368(6494):1016–1020. doi:10.1126/science.abb7015
43. Decaro N, Balboni A, Bertolotti L, et al. SARS-CoV-2 infection in dogs and cats: facts and speculations. *Front Vet Sci*. 2021;8:619207. doi:10.3389/fvets.2021.619207
44. Sila T, Sunghan J, Laochareonsuk W, et al. Suspected cat-to-human transmission of SARS-CoV-2, Thailand, July–September 2021. *Emerging. Infect Dis J*. 2022;28(7):1485–1488. doi:10.3201/eid2807.212605
45. Yen H-L, Sit TH, Brackman CJ, et al. Transmission of SARS-CoV-2 Delta variant (AY.127) from pet hamsters to humans, leading to onward human-to-human transmission: a case study. *Lancet*. 2022;399(10329):1070–1078. doi:10.1016/S0140-6736(22)00326-9
46. Evaluation for SARS-CoV-2 testing in animals. CDC. Accessed March 30, 2022. https://www.cdc.gov/coronavirus/2019-ncov/animals/animal-testing.html
47. Carvallo FR, Martins M, Joshi LR, et al. Severe SARS-CoV-2 infection in a cat with hypertrophic cardiomyopathy. *Viruses*. 2021;13(8):1510. doi:10.3390/v13081510
48. Rotstein DS, Peloquin S, Proia K, et al. Investigation of SARS-CoV-2 infection and associated lesions in exotic and companion animals. *Vet Pathol*. 2022;59(4):707–711. doi:10.1177/03009858211067467
49. Joint statement on the prioritization of monitoring SARS-CoV-2 infection in wildlife and preventing the formation of animal reservoirs. World Organisation for Animal Health. Accessed March 7, 2022. https://www.woah.org/en/joint-statement-on-the-prioritization-of-monitoring-sars-cov-2-infection-in-wildlife-and-preventing-the-formation-of-animal-reservoirs/
50. APHIS Veterinary Services. National list of reportable animal diseases. Accessed July 12, 2022. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/monitoring-and-surveillance/nlrad/ct_national_list_reportable_animal_diseases

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