Coronaviruses and cats

This paper provides an overview of coronaviruses and how they affect organisms across the animal kingdom, with a particular emphasis on cats. We review the latest evidence of pets testing positive for the novel coronavirus (SARS-CoV-2) causing COVID-19. Actionable advice on how to minimize the already low risk of your pet developing COVID-19 is also provided.
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How can we protect our pets from the consequences of COVID-19 infection in the family?

Sources
Coronaviruses - overview

Coronaviruses (CoVs) belong to the Coronaviridae family, part of the Nidovirales order of viruses. Viruses in the Nidovirales order share some common characteristics:

- The viruses’ genetic material is stored in a positive sense RNA form. This means that, when the virus enters the host organism’s cells, its viral genome hijacks the cell’s molecular machinery to start making viral proteins and copies of itself (resulting in infection).

- All viruses in this order have unusually large RNA genomes ranging from 26 to 32 kilo-base pairs (Kbps). For comparison, Ebola, also an RNA virus, has a genome size of 18 - 19 Kbps.

The Coronaviridae family consists of two subfamilies of viruses – coronaviruses and toroviruses. While toroviruses can infect both terrestrial and aquatic animals, coronaviruses target a more narrow selection of hosts - mammals and birds. CoVs get their name from their appearance – they have crown-like spikes on their surface (Figure 1) and come in 4 subgroups – alpha (α), beta (β), gamma (γ) and delta (δ). They can cause a variety of diseases including pneumonia, reproductive disease, enteritis, polyserositis, sialodacryoadenitis, hepatitis, encephalomyelitis, nephritis, and others. So far, CoV and CoV-like infections have been observed in pigs, cattle, horses, dogs, cats, camels, rodents, birds, bats, rabbits, ferrets and some wildlife species. While CoVs can cause serious diseases, many infections are subclinical (i.e., asymptomatic). When it comes to humans, CoVs are on the spectrum of viruses known to cause the common cold, but also more severe respiratory diseases, such as severe acute respiratory syndrome (SARS), Middle Eastern respiratory syndrome (MERS), and COVID-19.

Figure 1
Pictorial illustration of a typical coronavirus. The organization of the spike (S), membrane (M), and envelope (E) glycoproteins is shown. The RNA is protected by the nucleocapsid proteins (N). Taken from Holmes and Enjuanes.
Coronaviruses across the animal kingdom

Multiple CoVs of veterinary significance have been described so far, spanning across all four CoV subgroups - alpha, beta, gamma, and delta. Table 1 presents the most prominent examples, alongside the affected animal species.

Table 1. Clinical characteristics of major coronavirus infections of veterinary significance (informed by James⁴ and Zhang et al.⁶)

<table>
<thead>
<tr>
<th>Coronavirus</th>
<th>Disease / symptoms</th>
<th>Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alphacoronavirus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feline enteric coronavirus</td>
<td>Mild gastroenteritis and diarrhea</td>
<td>🐱</td>
</tr>
<tr>
<td>Feline infectious peritonitis virus</td>
<td>Peritonitis, pneumonia, central nervous systems symptoms, etc.</td>
<td>🐱</td>
</tr>
<tr>
<td>Canine coronavirus</td>
<td>Mild gastroenteritis and diarrhea; possible severe enteritis and systemic signs (leukopenia)</td>
<td>🐶</td>
</tr>
<tr>
<td>Transmissible gastroenteritis (TGE) swine virus</td>
<td>Gastroenteritis, watery diarrhea, vomiting, dehydration</td>
<td>🐄</td>
</tr>
<tr>
<td>Porcine respiratory coronavirus</td>
<td>Mild respiratory disease or subclinical</td>
<td>🐷</td>
</tr>
<tr>
<td><strong>Betacoronavirus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Porcine hemagglutinating encephalomyelitis virus</td>
<td>Vomiting, wasting disease, encephalomyelitis, anorexia, hyperesthesia, muscle tremors, emaciation</td>
<td>🐷</td>
</tr>
<tr>
<td>Mouse hepatitis virus</td>
<td>Enteritis, hepatitis, demyelinating encephalomyelitis</td>
<td>🐭</td>
</tr>
<tr>
<td>Rat sialodacryoadenitis virus</td>
<td>Rhinitis, epiphora, pneumonia</td>
<td>🐭</td>
</tr>
</tbody>
</table>
In most cases, CoVs give rise to infections that do not cross the inter-species barriers, meaning that the feline infectious peritonitis virus, for example, cannot infect other animal species or humans. However, every once in a while, certain CoVs mutate in a way that allows transmission from one species to another. This is the case with SARS-CoV, MERS-CoV and, most recently, SARS-CoV-2, the virus causing COVID-19. These viruses are considered zoonotic (i.e., originating in animals, but capable of infecting humans).

In the cases of SARS-CoV and MERS-CoV, scientists believe that they each originated in bats (the reservoir species), but transitioned through an intermediate animal host, such as civets and camels, respectively, before they made the evolutionary jump to being able to infect humans. When it comes to SARS-CoV-2, recent findings indicate that the host species of origin was also bats, with the virus passing through pangolins on its way to humans.

<table>
<thead>
<tr>
<th>Virus Species</th>
<th>Clinical Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine coronavirus</td>
<td>Gastroenteritis with profuse or bloody diarrhea, dehydration, decreased milk, or respiratory disease</td>
</tr>
<tr>
<td>Equine coronavirus</td>
<td>Gastroenteritis</td>
</tr>
<tr>
<td>Canine respiratory coronavirus</td>
<td>Respiratory disease</td>
</tr>
<tr>
<td>Severe acute respiratory syndrome (SARS) CoV</td>
<td>Respiratory disease; zoonotic, with bats as a natural reservoir</td>
</tr>
<tr>
<td>Middle East respiratory syndrome (MERS) CoV</td>
<td>Respiratory disease; zoonotic, with bats and camels as a likely reservoir</td>
</tr>
<tr>
<td>Novel coronavirus SARS-CoV-2 (COVID-19 disease)</td>
<td>Respiratory disease; zoonotic, with bats and pangolins as a likely reservoir</td>
</tr>
<tr>
<td>Avian infectious bronchitis</td>
<td>Tracheobronchitis, nephritis, rales, decreased egg production</td>
</tr>
<tr>
<td>Turkey coronavirus, Bluecomb virus</td>
<td>Enteritis, diarrhea, depression, cyanotic skin</td>
</tr>
<tr>
<td>Porcine deltacoronavirus</td>
<td>Gastroenteritis in sows and nursing pigs; low mortality in nursing pigs; clinically indistinguishable from TGE and PEDv</td>
</tr>
</tbody>
</table>
Coronaviruses and cats

Feline enteric coronavirus (FECV)

FECV is a highly prevalent virus in domestic cat populations across the world, although the infection is often either subclinical or marked by mild gastrointestinal illness in kittens. Around 40% of cats in single households and 90% of cats in a multicat environment had, at some point, been exposed to the virus. In rare cases, the infection can be accompanied by acute or chronic vomiting and diarrhea not responding to treatment and, even less frequently, by upper respiratory tract symptoms. If symptoms are mild, therapy will most likely not be administered. When symptoms are severe, treatment includes fluid therapy, oral electrolyte solutions and antiemetics; no targeted antiviral therapy exists for FECV.

The route of infection is through ingestion or inhalation of feces containing FECV or through contact with contaminated litter boxes, housing, etc. The chance of transmission increases when cats are kept in close contact with each other, as is the case in houses with multiple cats and catteries with limited space. Active infection prevention is mostly a concern in catteries and rescue shelters, not ordinary households. Some precautionary measures include: having adequate litter for the number of cats housed in the same place, daily litter box cleaning and weekly disinfection.
Feline infectious peritonitis (FIP) virus

A small percentage of cats infected by FECV (5-10%) develop clinical infectious peritonitis (a highly fatal disease affecting multiple systems), at which point the virus is referred to as feline infectious peritonitis virus (FIPV). FIP results from infection with genetic variants of FECV that have acquired the ability to replicate within macrophages and thus evade destruction by these immune cells. This causes infected macrophages to form perivascular clusters in various organs and tissues and serve as viral incubators, where their high viral content attracts even more macrophages in an attempt to destroy the virus. This results in a strong, but ineffective immune response where the virus keeps replicating and organs get damaged.

No single FECV genome mutation has been associated with the development of FIP. It is still unclear whether cats that develop FIP are infected with FECV which mutates into FIPV inside their organism or whether those cats get infected with an already virulent strain of FECV. Most likely, the interplay between viral genetics and the individual cat’s immune response is what influences the chance of developing FIP.

The disease usually occurs in young or senior cats, or in cats with compromised immunity. At the onset, clinical symptoms include anorexia, chronic fever, malaise, weight loss, and, in some cases, ocular and neurological symptoms. There are two clinical forms of FIP - ‘wet’ form (characterized by abdominal effusion) and ‘dry’ form (lacking abdominal effusion). In the classical wet form, in addition to the already mentioned symptoms, viscous liquid accumulates in the peritoneal cavity, resulting in abdominal enlargement (Figure 2), visible to the naked eye. This form of the disease has a very rapid progression, with death within weeks or months. The dry form of the disease typically progresses more slowly.
There is no highly effective vaccine for FIPV currently available on the market. The only commercially available vaccine has limited efficacy in cats that had already been exposed to FECV in the past (most cats). However, efforts are underway to develop a more effective vaccine - researchers at Colorado State University are currently working on a new vaccine for FECV, a project funded by the Morris Animal Foundation. In addition, there have been some recent advancements in FIP prevention through a non-vaccine based approach. The supplement Mutian X, typically prescribed for cats suffering from FIP, was tested on cats that have an asymptomatic FECV infection. Twenty-nine such cats stopped shedding the virus in their feces following treatment with Mutian X. These findings suggest that Mutian X could be used to decrease the probability of propagating FECV transmission and subsequent FIP development if used in multicat households, catteries, and shelters.

Currently, treatment options for FIP are limited and mostly palliative, although two new therapies in development have shown some promise. While the therapies have not been approved yet, they are already distributed on the black market as treatments for FIP. GC376 was the first antiviral compound evaluated for treating FIP. The drug led to initial improvement in 19 out of 20 cats with FIP within the first 2 weeks of treatment initiation, although 13 out of the 19 cats relapsed and failed to respond to further treatment with GC376. Treatment also interfered with permanent teeth development in young cats. The second drug, GS-441524, demonstrated a satisfactory safety profile, while successfully treating 25 out of 31 cats included in a clinical trial (repeated treatment was necessary in relapsed cases).

Figure 2.
Abdominal enlargement associated with the wet form of feline infectious peritonitis (taken from Hartmann).
COVID-19 and cats

With the evolving COVID-19 pandemic, reports of 2 dogs in Hong Kong, 1 cat in Belgium, and 1 tiger in New York infected with SARS-CoV-2 have emerged in the news. The first dog was a 17-year-old Pomeranian with multiple comorbidities and was owned by a COVID-19 patient. Oral and nasal cavity samples from the dog tested weakly positive for SARS-CoV-2 in five separate molecular tests (RT-PCR based) over a 2-week period, suggesting a weak and asymptomatic, but true infection. It is also important to mention that when two other types of tests for COVID-19 were used (culture-based and serological), the dog tested negative. A key implication of these results is that, while the RNA of the virus was present in the dog’s system (as evidenced by the RT-PCR tests), the dog never developed antibodies against it, meaning that the virus never caused a potent immune response. The second dog that tested positive for COVID-19 was a 2-year-old German shepherd and was also owned by a COVID-19 patient.

Similarly, the cat that tested positive for COVID-19 was owned by a COVID-19 patient. The cat started exhibiting symptoms a week after its owner contracted the disease. However, it is unclear whether the symptoms of diarrhea, vomiting and breathing difficulties were all related to COVID-19, as not much is known about other comorbidities the cat might have been suffering from.

Surprisingly, the New York Zoo recently reported that a tiger had tested positive for SARS-CoV-2 after showing symptoms of respiratory illness. As are the cases of the cats and dogs testing positive for the virus, it is believed that the tiger became infected after interacting with a person (zoo employee) who already had the disease.
Probably the most noteworthy currently available information regarding cats’ susceptibility to COVID-19 comes from the first scientific study on the matter, available in pre-print from a group of Chinese scientists. The researchers found that the SARS-CoV-2 virus seems to replicate poorly in dogs, pigs, chicken, and ducks, but potentially more efficiently in ferrets and cats. To study the effect of SARS-CoV-2 on cats, five 8-month-old cats were deliberately inoculated intranasally with the virus. SARS-CoV-2 RNA was detected in the nasal turbinates, soft palates, tonsils, trachea and small intestine of all 5 deliberately inoculated cats (with some variation in the positive tissue types across cats). The lung tissue was not positive for the virus. Evidence of infectious viral particles (not just viral RNA) was seen in two of the cats, indicating active infection.

In the second part of the experiment, scientists placed three healthy cats in close proximity to three of the virus inoculated cats to test whether infected cats can transmit the virus to other cats. Only one of the three non-inoculated cats tested positive for the presence of SARS-CoV-2 RNA. This indicates that, in some cases, infected cats can transmit the disease to other cats.

Although intriguing, it is important to note a few key points about this study and its results:

- No negative controls were included in the study’s design. Negative controls are necessary to judge the rate of false positive results occurring with the viral detection assays that were used.
- The study’s conclusions are based on a small sample size.
- The viral inoculation conditions used in this study rely on very high doses of the virus and are not representative of what happens during normal interactions between an infected human and their cat.
- None of the infected cats showed any symptoms.
- There is no evidence that infected cats can transmit the disease to humans or that they have been or will be a critical driving force in the COVID-19 pandemic.

All of these points should be given their due consideration when interpreting the study’s results and their implications. “The overwhelming consensus is that our pets pose no particular threat to infecting us with the novel coronavirus,” said veterinarian physician Ernie Ward in his blog reviewing the study. This conclusion is further supported by the findings that the closely related SARS-CoV virus that caused an epidemic in 2003 was also able to infect cats, but no evidence of cats infecting humans was ever demonstrated.
How can we protect our pets from the consequences of COVID-19 infection in the family?

Various sources, including the Center for Disease Control and Prevention (CDC), the American Veterinary Medical Association (AVMA), and prominent veterinarians have put together guidelines to help minimize the already relatively small risk of COVID-19 infection in pets20,22,23.

Advice includes:

- If you are confirmed to have COVID-19, you should keep yourself isolated not only from other people, but also from pets. If you must continue daily pet care, it is advised that you wear a facemask when performing care duties or show affection to the pet and wash your hands before and after contact.

- If you do not have COVID-19, you can continue interacting with your pet as before, but practice good hygiene - wash your hands before and after any interaction and regularly clean the pet's bowls, toys, etc.

- Restrict your pet's contact with other animals and people outside the household.

- Bathe your pet after any contact with a potentially infectious person.

- Restrict your cat's outdoor activities.

- Wash your hands after touching other people's pets.

- It is recommended to have an emergency plan for your pet in case you contract COVID-19. Zoetis Petcare suggests the following24:
  - Designate an alternative pet care provider in case you become ill.
  - Keep your pets up-to-date with their vaccine schedule and have a well-organized folder with their health records stored in a safe place.
  - Create a pet preparedness kit. More information on what to include in the kit can be found at: https://www.cdc.gov/healthypets/emergencies/pet-disaster-prep-kit.html
Sources


16) https://veterinaryrecord.bmj.com/content/186/12/388.2


20) https://www.dreierneward.com/blog/catsandcoronavirus


Be safe.
Stay Home.
Home is where the cats are.