

# **Scientific Assessment of the Zoonotic Potential of COVID-19**

**Updated: Mar. 6, 2020**

*This document summarizes what is currently known about COVID-19 from a zoonotic perspective and provides additional background on coronaviruses to support animal-related assessment of risk*

## **WHAT'S NEW:**

- Other modes of transmission in humans (e.g. fecal-oral, asymptomatic) may be possible
- Hong Kong recently reported a pet dog testing weakly positive for SARS-CoV-2 via RT PCR
- Further research on pangolins as intermediate hosts has been released but conclusions vary and further research is needed; other research has proposed turtles as a possible intermediate host

## **KEY POINTS**

### **ANIMAL RESERVOIR:**

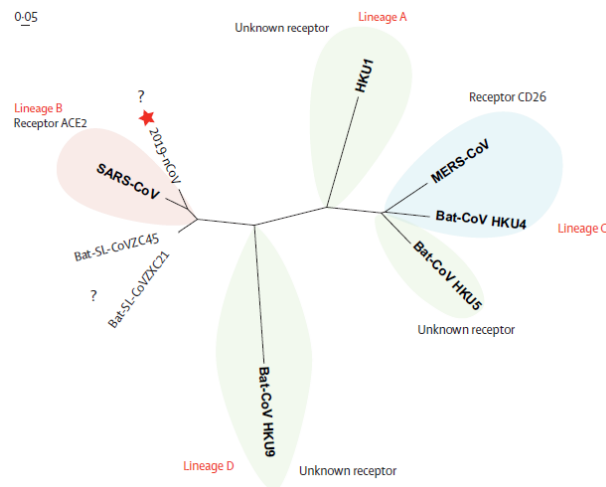
- COVID-19 was first recognized in a cluster of human pneumonia cases associated with the Huanan Seafood Wholesale Market in Wuhan City, China. A number of environmental samples at the market were positive, particularly where wildlife trading occurred. Samples were taken from several species of animals and [none of these samples tested positive](#); information about the number of samples and species sampled is not available.
- Several studies have found that COVID-19 is closely related genetically to Chinese horseshoe bats, making them a likely reservoir (Chan et al., 2020; Zhu et al., 2020).
- However, it is suspected that another animal acted as an intermediate host between bats and humans. Recent research has proposed several different animal species (i.e. snakes, pangolins, and turtles) but all remain to be proven (Ji et al., 2020; Xiao et al., 2020; Lam et al., 2020; Liu et al., 2020; Zhang et al., 2020; Wahba et al., 2020; Wong et al., 2020; Liu et al. 2020).

### **ANIMAL HOST RANGE:**

- Dogs: On Feb. 28, 2020, the Government of Hong Kong announced that a pet dog of a COVID-19 case had tested positive for the virus. Oral and nasal swabs had tested weak positive by real time RT-PCR and two subsequent follow-up tests were also positive. Experts, including the OIE, concluded that the [dog has a low-level of infection](#). The dog has not shown any clinical signs of illness. It is likely a case of human to animal transmission. There is currently no evidence that dogs can spread the infection.
- Other animal species: A recent study found that pigs, ferrets, cats, and non-human primates have ACE2 receptors that are favourable for COVID-19 binding (Wan et al., 2020). This is similar to what has previously been found for SARS-CoV (see in background below). The ACE2 receptor is relatively conserved across mammals (Graham et al., 2010).

## COVID-19 VIRUS CHARACTERISTICS

- The COVID-19 virus is a betacoronavirus, subgenus sarbecovirus, lineage B and closely related genetically to SARS-related coronaviruses found in Chinese horseshoe bats (Chan, et al. 2020; Zhu et al., 2020).
- The sequence is about 79% identical to SARS-CoV and 50% to MERS-CoV (Lu et al., 2020).
- COVID-19 uses the host cell receptor ACE2, the same receptor as SARS (Zhou et al., 2020 [pre-print], Wan et al., 2020).



Phylogenetic analysis of the receptor binding domain (RBD) of various betacoronaviruses. From Lu et al., 2020.

## TRANSMISSION

- COVID-19 is predominantly spread person-to-person by respiratory droplets, through close contact or by fomites, similar to SARS (WHO, 2020).
- **Recent research suggests that COVID-19 may also be spread through the fecal-oral route, although likely less commonly (WHO, 2020).**
- Research into asymptomatic transmission is ongoing however it is known that it is possible for people with only very mild symptoms to spread the virus to others (WHO, 2020).

## ANIMAL RESERVOIR

- COVID-19 was first recognized in a cluster of human pneumonia cases associated with the Huanan Seafood Wholesale Market (also known as the South China Seafood Market) in Wuhan City, China and is therefore thought to have originated from an animal source at this market. A number of different animal species have been reported to have been sold at this market

including tiger frogs, snakes, hedgehogs, civets, peacocks, deer, wild mangosteens, cats, arrow pigs, dogs, mink, marmots, bats, birds, rabbits, and wolf cubs.

- **Bats and COVID-19:** Several studies have been published recently finding that COVID-19 is closely related genetically to Chinese horseshoe bats. A study recently published by Chan et al. (2020) conducted phylogenetic analysis of virus isolated from COVID-19 patients and determined that this virus is most closely related to the bat SARS-related coronaviruses previously found in Chinese horseshoe bats. Another recently published study by Zhu et al. (2020) also found the virus to be similar to some coronaviruses found in bats. Other currently unpublished phylogenetic analyses support the finding of bats as the likely reservoir.
- A study from Ji et al. (2020) report findings indicating bats and snakes as possible sources. However, the methods used in this study are not sufficient on their own to implicate snakes as the source of the outbreak and there is some controversy within the scientific community about the results.
- Although bats are a likely reservoir, it is also suspected that another animal is acting as an intermediate host between bats and humans. Phylogenetic analysis indicates that bats are not a direct ancestor of COVID-19 (<90% identical). Additionally, bats hibernate during the winter (when this outbreak was first reported), bats were not reported to be sold at the market, and the similar viruses SARS-CoV and MERS-Cov both had intermediate hosts between bats and humans (Lu et al., 2020).
- On January 26, 2020 it was announced that 33/585 samples collected on Jan. 1 and Jan. 12, 2020 from the South China Seafood Market were positive for the virus by PCR. The positive samples were from 22 stalls and one garbage truck and almost all were from the western area of the market where wildlife trading occurs.
- Due to this finding, that same day (January 26, 2020) Chinese authorities issued an announcement prohibiting wild animal trading until the end of the epidemic to “cut off the source and transmission of the virus”.
- **Pangolins and COVID-19:** on February 7, 2020, researchers in China announced that the pangolin is a potential intermediate host for the novel coronavirus (<https://www.scau.edu.cn/2020/0207/c1300a219015/page.htm>). It was reported that scientists tested more than 1000 animals and found viruses from pangolins were very closely related genetically (99%) to those from COVID-19 patients. A preprint article (prior to peer-review) of this research appears to now be available (Xiao et al., 2020). Researchers first used the whole genome sequence of COVID-19 virus in a BLAST search of SARS-like CoV sequences in all available mammalian and avian viromic, metagenomic, and transcriptomic data which identified 34 highly related contigs in a set of pangolin viral metagenomes. They then analyzed pangolin samples (from 4 Chinese pangolins and 25 Malayan pangolins that were collected from a wildlife rescue center) for SARSr-CoV using RT-PCR with primers targeting a conservative region of  $\beta$  CoV. They found 17/25 Malayan pangolins positive by PCR and 1/8 serum samples positive for

antibodies. Coronavirus isolated from these Malayan pangolins (Pangolin-CoV) showed 100%, 98.2%, 96.7% and 90.4% amino acid identity with 2019-nCoV in the E, M, N and S genes, respectively. They also found that the RBD of the S protein of Pangolin-CoV has only one amino acid difference from that of COVID-19. They then concluded from this that COVID-19 virus might have originated from the recombination of a Pangolin-CoV-like virus with a Bat-CoV-RaTG13-like (horseshoe bat) virus and that pangolins have the potential to act as the intermediate host of 2019-nCoV.

- A pangolin is an endangered mammal considered to be a delicacy in China and also used in traditional medicine. It is illegal to trade or sell pangolins however it is one of the world's most heavily trafficked animals. Coronaviruses have previously been found in pangolins (Liu et al., 2019).
- Several other preprint articles investigating pangolins and COVID-19 are also now available. Although they all have found that coronaviruses in pangolins are very similar genetically to SARS-CoV-2, the pangolin's role as an intermediate host remains to be proven (Lam et al., 2020; Liu et al., 2020; Zhang et al., 2020; Wahba et al., 2020; Wong et al, 2020).
- On February 20, 2020 a ProMED post of a Chinese media article (February 15, 2020 - <https://tinyurl.com/sehot3r>) reported that “the Chinese Center for Disease Control and Prevention's Virology Institute tested 585 environmental and animal samples from the Huanan Seafood Market” as well as “the team of the China Animal Health and Epidemiology Center tested more than 4800 animal samples collected from pigs, poultry, dogs, and cats in recent years, all of which were negative”. This is the first report of animals being tested (vs only environmental samples) although more information is needed to understand this testing.
- **On February 24, 2020, China passed a proposal for a permanent wild animal trade and consumption ban (<https://www.dailymail.co.uk/news/article-8037093/China-considers-complete-ban-eating-wild-animals-amid-coronavirus-outbreak.html>).**
- **A study from researchers in China (Liu et al. 2020) has suggested that turtles could be possible intermediate hosts of the COVID-19 virus (along with pangolins). The study looked at the RBD of the S-protein of SARS-CoV-2 and the ACE2 receptor of turtles (as well as pangolins and bats) and found fewer amino acid mutations in one area of ACE2 receptor in turtles and pangolins than bats (although more than humans and non-human primates). Coronaviruses have not been reported in turtles and more research is needed. (<https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25726>)**

## HOST RANGE

- The ACE2 receptor is relatively conserved across mammals (Graham et al., 2010).
- A recent study found that pigs, ferrets, cats, and non-human primates have ACE2 receptors that are favourable for COVID-19 binding (Wan et al., 2020).

- On January 30, 2020, Li Lanjuan, an epidemiologist and a member of the high-level expert team on the novel coronavirus convened by the National Health Commission mentioned in an interview that COVID-19 is transmitted from mammal to mammal and therefore people should monitor their pets and quarantine them if they have had contact with someone who is sick (<https://www.chinadaily.com.cn/a/202001/30/WS5e3274a4a310128217273b43.html>). At this time there were not any reports of pets or other animals testing positive for COVID-19 so this may have been a precautionary message. However, since then there have been several media reports of fear towards dogs and cats in China resulting in the inhumane treatment of animals.
- **Hong Kong reports dog testing positive for COVID-19: On Feb. 28, 2020, the Government of Hong Kong announced that a pet dog of a COVID-19 case has tested positive for the virus. Oral, nasal, and rectal swabs were collected from the dog and the oral and nasal swabs tested weak positive on Feb. 27 but follow-up testing on Feb. 28 and Mar. 2 was also positive leading experts to conclude that this dog has a low-level infection. The dog is in quarantine and further follow-up tests will be conducted.**  
[https://www.oie.int/wahis\\_2/public/wahid.php/Reviewreport/Review?page\\_refer=MapFullEventReport&reportid=33455&newlang=en](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport/Review?page_refer=MapFullEventReport&reportid=33455&newlang=en).  
<https://www.info.gov.hk/gia/general/202003/04/P2020030400658.htm?fontSize=1>.

#### Other Relevant Media/Websites

- Several organizations (including PHAC) now have information available on their websites in regards to animals and COVID-19:
  - PHAC – <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/frequently-asked-questions.html>
  - US CDC – <https://www.cdc.gov/coronavirus/2019-ncov/faq.html#2019-nCoV-and-animals>
  - World Organization for Animal Health (OIE) – <https://www.oie.int/en/scientific-expertise/specific-information-and-recommendations/questions-and-answers-on-2019novel-coronavirus/>
  - WHO – <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>
  - ECDC – <https://www.ecdc.europa.eu/en/novel-coronavirus-china/questions-answers>
  - World Small Animal Veterinary Association (WSAVA) – [https://wsava.org/wp-content/uploads/2020/02/nCOV\\_WSAVA-Advisory-Documents-final-05.02.2020.pdf](https://wsava.org/wp-content/uploads/2020/02/nCOV_WSAVA-Advisory-Documents-final-05.02.2020.pdf)

This situation is evolving and new information is available daily. This summary will continue to be updated as required.

## **Background on Coronaviruses**

### **Virus**

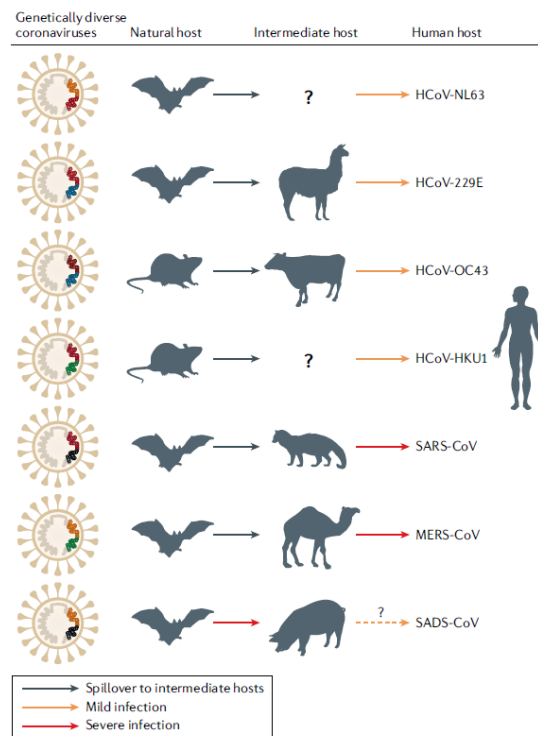
- Coronaviruses are a large family of viruses that can cause disease in humans as well as several different animal species.
- Coronaviruses are enveloped, positive-sense, non-segmented, single-stranded RNA viruses.
- They are classified into four genera:
  - Alphacoronaviruses
  - Betacoronaviruses
  - Gammacoronaviruses
  - Deltacoronaviruses
- The alphacoronaviruses and betacoronaviruses infect only mammals. The gammacoronaviruses and deltaxoronaviruses infect primarily birds, but some of them can also infect mammals (Woo et al., 2012).
- Human coronaviruses were first identified in the mid-1960s. The four common coronaviruses that typically cause mild upper respiratory infections in people include:
  1. 229E (alphacoronavirus)
  2. NL63 (alphacoronavirus)
  3. OC43 (betacoronavirus)
  4. HKU1 (betacoronavirus)
- Other previously identified human coronaviruses that can cause severe disease include:
  5. MERS-CoV (betacoronavirus)
  6. SARS-CoV (betacoronavirus)
- Human and animal coronaviruses are globally distributed.

### **Transmission**

- Human coronaviruses are primarily transmitted person-to-person through direct contact with secretions, through fomites, or via respiratory droplets. They have also been detected in faeces and urine and, under certain circumstances, transmission can occur from aerosolised respiratory secretions and faecal material (PHAC, 2010 and 2019a).
- In temperate climates, coronavirus respiratory infections occur primarily in the winter with smaller peaks in autumn or spring (Hendley et al., 1972).
- Ongoing zoonotic transmission occurs in some instances such as MERS-CoV which can be transmitted from dromedary camels to people, usually through direct contact (PHAC, 2019b). Raw camel milk and raw/undercooked camel meat is also considered a risk for possible transmission of MERS (Gossner et al., 2016).

## Animal Reservoir/Host Range

- A wide range of wild and domesticated animal species are host to coronaviruses worldwide:
  - Alphacoronaviruses – e.g. feline infectious peritonitis virus, porcine transmissible gastroenteritis virus, porcine epidemic diarrhea virus, several bat coronaviruses.
  - Betacoronaviruses – e.g. murine hepatitis virus, bovine coronaviruses, rat sialodacryoadenitis virus, porcine hemagglutinating encephalomyelitis virus, canine respiratory coronavirus, equine coronavirus, several bat coronaviruses.
  - Gammacoronaviruses – avian viruses such as infectious bronchitis virus and a coronavirus isolated from a captive beluga.
  - Deltacoronaviruses – avian viruses and one from pigs (one case) although they have not been associated with disease.
- Pathogenic animal coronaviruses typically cause respiratory or enteric infections.
- Betacoronaviruses are particularly known to cross between species (Boileau & Kapil, 2010).
- On the basis of current sequence databases, all human coronaviruses have animal origins:
  - SARS- CoV, MERS- CoV, NL63 and 229E are considered to have originated in bats;
  - OC43 and HKU1 likely originated from rodents (Cui et al., 2019)



Animal reservoirs of human coronaviruses. From Cui et al., 2019

- Mutation and genetic recombination appears to occur frequently within coronaviruses, especially in the genes encoding the spike protein (Holmes, 2005; Su et al., 2016).

- The spike protein, in particular the receptor binding domain (RBD) of the spike protein, appears to be the most important factor in determining host range (Holmes, 2005; Graham et al., 2010). Infection occurs when the spike protein binds to a receptor on the host cell.
- SARS-CoV uses the host cell receptor angiotensin converting enzyme 2 (ACE2). Based on studies of SARS-CoV it appears that very few amino acid substitutions in the RBD would be required for adaption to the ACE2 receptor of a new host species (Holmes, 2005).
- However, other mutations in genes for virus replication and transmission are also required to successfully adapt to a new host (Holmes, 2005).
- Generally, coronaviruses that have made species jumps have lost their capacity to infect the animals in which they were originally found (Müller et al., 2012).

## SARS

- During and following the SARS epidemic of 2002-2003, several different animal species were investigated. Ultimately, it was found that SARS-CoV jumped from bats to palm civets (wild cat-like carnivores) before being transmitted to humans (Guan, 2003; Wang & Eaton, 2007; Field, 2009). Other research found:
  - Investigation into an outbreak of SARS in 2003 in an apartment complex in Hong Kong where more than 300 residents were infected found viral remnants in 4/8 samples of rat droppings and in the throat or rectal swabs of 5 housecats, 1 dog, and at least 1 rat. One of the cats was also found to have SARS antibodies. (Ng, 2003)
  - Another 2003 study in China looked for the presence of SARS in pigs, cattle, dogs, cats, chickens, and ducks on a farm. SARS antibodies were detected in 2/108 pigs (no clinical signs) and virus was isolated from one of them. Sequence and epidemiology analyses suggested that the pig was infected by a virus of human origin, possibly through being fed garbage from restaurants. SARS antibodies or virus was not detected in any of the other animals tested. (Chen et al., 2005)
  - Experimental infection with SARS-CoV caused clinical disease in macaques (Fouchier, et al., 2003) and ferrets and subclinical infection in cats (Martina et al., 2003). The infected ferrets and cats were also able to transmit SARS-CoV to uninfected cage mates (Martina et al., 2003).
  - Experimental infection of chickens and pigs with SARS-CoV by The CFIA National Centre for Foreign Animal Disease found antibodies in pigs (no clinical or gross pathological signs) and viral RNA in both species, however they were unable to isolate the virus. (Weingartl et al., 2004)
  - A survey conducted at a China market in 2004 before the mass culling of palm civets (the intermediate reservoir of SARS) found cats, red foxes, a rat and a wild boar positive by RT-PCR however since the environment was heavily contaminated at that time it is



not known whether these animals were actually susceptible hosts or only mechanical vectors (Wang et al., 2005).

- In finding a suitable animal model for SARS, some rodent species have been found to be able to be infected experimentally (Shi et al., 2008).

## **MERS**

- Dromedary camels have been confirmed by several studies to be the natural host and zoonotic source of the MERS-CoV infection in humans. It has been associated with mild upper respiratory signs in some dromedary camels (OIE, 2019).
- Beyond camels, research to date has only found natural MERS-CoV infection in alpacas, although they are asymptomatic (Reusken et al., 2016). Investigations into other animal species have found:
  - Serological testing of domestic livestock (cattle, sheep, goats, and chickens) in Saudi Arabia did not detect any antibodies to MERS-CoV (Hemida et al., 2013)
  - Serological testing of domestic livestock (cattle, sheep, goats) in the Middle East (Oman), Spain, Netherlands, and Chile also did not detect any antibodies to MERS-CoV (Reusken et al., 2013).
  - Serological testing of horses from United Arab Emirates and Spain did not detect any exposure to MERS-CoV (Meyer et al., 2015).
  - Serological testing of animals (water buffaloes, cattle, sheep, and goats) in Egypt were also negative for MERS-CoV antibodies (Perera et al., 2016).
- Experimentally, rhesus macaques, marmosets, and rabbits have been shown to be susceptible to infection (PHAC, 2019b).

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