COVID-19: A Veterinary and One Health Perspective

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Abstract | Interface with animals has been responsible for the occurrence of a major proportion of human diseases for the past several decades. Recent outbreaks of respiratory, haemorrhagic, encephalitic, arthropod-borne and other viral diseases have underlined the role of animals in the transmission of pathogens to humans. The on-going coronavirus disease-2019 (COVID-19) pandemic is one among them and is thought to have originated from bats and jumped to humans through an intermediate animal host. Indeed, the aetiology, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can infect and cause disease in cats, ferrets and minks, as well as be transmitted from one animal to another. The seriousness of the pandemic along with the zoonotic origin of the virus has been a red alert on the critical need for collaboration and cooperation among human and animal health professionals, as well as stakeholders from various other disciplines that study planetary health parameters and the well-being of the biosphere. It is therefore imminent that One Health principles are applied across the board for human infectious diseases so that we can be better prepared for future zoonotic disease outbreaks and pandemics.

1 Introduction
The COVID-19 pandemic is a stark reminder that we live in a time where pathogens spread faster than we can track them. The incidence of other diseases in humans such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS),1 H1N1 pandemic influenza,2 H5N1 avian influenza,3 Ebola haemorrhagic fever,4 etc. in just the last two to three decades has also highlighted that globalization and animal–human interface are major factors in the transmission of pathogens from wild and domestic animals to humans.

Recent advances, especially in genomics, have spurred the understanding of diseases in terms of their aetiology, origin, identification of index case, routes of spread and potential transmission, evolution of the pathogen, minutest details of host–pathogen interaction and pathogenesis, and vaccine and/or drug discovery, facilitating disease mitigation strategies. At least one new infectious disease is thought to emerge or re-emerge every year.5,6 Between 1940 and 2004, there were 335 emerging infectious diseases, about 60% of them originating from animals, with not much change in decade-wise proportion of zoonotic diseases.7 About three-fourths of all emerging and re-emerging human diseases can be traced back to animals, particularly wild animals,7 and it has been propounded, probably rather radically, that every species of Kingdom Animalia may be a potential carrier of human pathogens.8

2 SARS-CoV-2 and Its Origin
The SARS-CoV-2 belongs to the family Coronaviridae and has one of the largest single-stranded RNA genomes (29.9 kilo bases) for a virus. The major structural proteins encoded by SARS-CoV-2 are spike (S), nucleoprotein, envelope and membrane proteins. Among these structural
proteins, the S protein is critical for the receptor-mediated entry of the virus into susceptible cells. The receptor binding domain (RBD) of the S protein binds the cellular receptor, the angioten-sin converting enzyme-2 (ACE2), 9 facilitating entry of the virion particle. Further, transmembrane protease serine 2 (TMPRSS2) helps in the priming of the S protein, where the S protein is cleaved so as to allow the fusion of viral envelope with cellular membrane. 9 In vitro, ACE2 from as many as 44 mammals has been shown to bind to the RBD. 10, 11 On the other hand, modelling studies have returned supporting as well as conflicting results on the interaction between S and ACE2. 12–15 Together, these studies only suggest interactions while receptor expression and other host factors may dictate infection, replication and pathogenesis as well as transmission to other hosts.

The first cases of COVID-19 are thought to have originated from live animal markets in Wuhan, China. Analysis of the genomes of SARS-CoV-2 has suggested that the virus may have originated from the Asian bats belonging to the Rhinolophus species 16–19 and that the transmission to humans may have involved an intermediate host, possibly the pangolin. 16, 17, 20–23 However, both the precise origin and the exact intermediate host are conjectures at best. On the other hand, higher sequence similarities of SARS-CoV-2 with bat coronavirus-RaTG13 (96.2%) and Guangdong Pangolin-CoV (92.4%) 22, 24 support the zoonotic origin of the virus. However, the SARS-CoV-2 has a unique “PRRA” motif at the junction of the S1 and S2 subunits of the S protein, which makes it distinct from RaTG13 or the Guangdong Pangolin-CoV. Further, the binding affinity of pangolin ACE2 receptor with RBD has been shown to be low. 25 Recent genetic analysis has revealed that three viruses in bats from the limestone karstic terrain in North Laos, BANAL-52, BANAL-103 and BANAL-236 are very close to SARS-CoV-2 with only one or two mutations in the RBD and the absence of a cleavage site for the cellular enzyme furin. These viruses are therefore considered to be the closest match to SARS-CoV-2 in nature. 26

3 Animal Models for SARS-CoV-2 Infection

Experimental reproduction of COVID-19 in mice requires adaptation of SARS-CoV-2 through serial passage 27 as wild-type mice are resistant to infection. 28 However, mouse adaptation also leads to changes in SARS-CoV-2, which is not ideal for challenge studies. When mutations relevant to mouse adaptation were introduced through reverse genetics, the resultant virus replicated in the upper and the lower respiratory tract of BALB/c mice when the virus was administered intranasally. 29 The main reason for the species restriction appears to be the receptor, since SARS-CoV-2 not adapted to mice or adapted to grow in cell culture can efficiently infect transgenic mice expressing human ACE2 (hACE2), 28–31 and such mice are considered suitable for challenge studies. Some transgenic mice such as HHF4-hACE2 mice express the receptor in the respiratory tract and the central nervous system, resulting in lethal encephalitis upon infection through the respiratory route. 29, 30, 32 A sole study has also reported that when administered intrastragically, the virus could potentially be transmitted by the faecal–oral route 33; however, the implications of this to transmission in humans are not clear, although SARS-CoV-2 causes gastroenteritis and is excreted in the faeces in humans, but faecal–oral transmission needs further evidence. 34

Transient expression of hACE2 has also been employed for mouse infection studies. This method has the advantage of utilizing mice from diverse genetic backgrounds. Adenovirus or adenovirus-associated virus-mediated transduction has been used to express hACE2 in the respiratory tract of mice. 35, 36 When mice were transduced with human adenovirus 5 expressing hACE2 and subsequently infected with SARS-CoV-2 through intranasal or intranasal and intravenous route, only the peripheral and not the systemic route resulted in lung infection in mice. 35 In mice transduced with adenovirus-associated virus 9 expressing hACE2, the transcriptome profile mimicked those in COVID-19 patients, in that interferon (IFN)-stimulated genes and inflammatory cytokines were up-regulated during SARS-CoV-2 infection. It was also observed that type I IFNs were responsible for pathological changes rather than controlling SARS-CoV-2 replication. 36

Unlike mice, hamsters are susceptible to SARS-CoV-2 infection without the need for adaptation of the virus. 30, 37, 38 Upon infection, hamsters lose weight initially but regain it by 14 days post-infection. Highest viral loads are detected in the nasal turbinates, lungs and trachea, facilitating the transmission of the virus to in-contact hamsters. 37 Similar to humans, aerosol and droplet transmission between hamsters was higher with the D614G mutant of the virus. 30

Two mustelids, which are used for commercial (minks) or experimental (ferrets) purposes, are highly susceptible to SARS-CoV-2. Minks undergo efficient upper and lower respiratory
tract infection, with viral RNA being detected in the nasal turbinates, soft palates, tonsils, all lung lobes and submaxillary lymph nodes and infectious virus being detected in most of these samples. Severe pathological conditions are observed in infected minks with extensive and diffuse consolidation of the lungs. Nasal mucosa and submucosa of the vestibular, respiratory and olfactory regions show inflammatory infiltrates, epithelial degeneration and necrosis. Notably, the SARS-CoV-2-mediated respiratory system damage is similar to what is observed in severe human COVID-19 cases. Transmission of SARS-CoV-2 between minks through droplets has also been demonstrated.  

Ferrets are also suitable animal models. SARS-CoV-2-infected ferrets show infectious virus in the upper respiratory tract and virus is shed in saliva, urine and feces. Infected ferrets transmit the virus through respiratory droplets to direct and indirect contact ferrets. Similar to ferrets, raccoon dogs infected with SARS-CoV-2 shed the virus through nasal route, leading to infection of in-contact animals. However, the raccoon dogs do not show any clinical signs.

Experimentally, SARS-CoV-2 has also been shown to replicate in cats and be excreted in respiratory secretions, and infected cats can transmit the virus to co-housed cats. On the other hand, virus replication is poor in bank voles, cattle, dogs, pigs, chicken, ducks and tree shrews.

Experimental studies have also been carried out to study the SARS-CoV-2 infection in non-human primates (NHP). Infection produces acute respiratory distress and interstitial pneumonia in rhesus macaques, and severe pneumonia in baboons, but no clinical signs in cynomolgus monkeys. Irrespective of the clinical signs, SARS-CoV-2-infected NHPs show highest viral load in the upper and lower respiratory tract, indicating that NHP’s are a good model to study COVID-19 pathogenesis and protective efficacy of vaccines.

White-tailed deer produced subclinical infection upon intranasal administration of a SARS-CoV-2 isolate from a tiger, with the virus excreted in nasal secretions. Pregnant deer could transmit the virus through direct contact and vertically from doe to the foetus, with similar genome proportions in the tissues of the primary and in-contact animals and foetuses. Experimental infection of sheep with SARS-CoV-2 resulted in a mild infection and the viral RNA could be detected in nasal and oral swabs one day post-infection. However, the transmission of the virus from the infected sheep to naïve sheep was limited. Similar to white-tailed deer, when sheep were co-infected with two lineages of SARS-CoV-2, the ancestral lineage A appears to have less advantage over the α variant. However, these experiments have used 1:10 ratio of lineage A and α variant virus for the infection, making appropriate interpretation difficult.

Details of the experimental infection of SARS-CoV-2 in animals are compiled in Table 1.

## 4 Natural Infection of Animals with SARS-CoV-2

Till date, 31 countries have reported SARS-CoV-2 infection in more than ten animal species (Table 2). While most of the infections are reported from pet animals, outbreaks have also been reported from organized mink farms, and zoo and wild animals.

Several observations have established that pet animals can be infected by SARS-CoV-2 (Table 2). Tests on 17 dogs and 8 cats from COVID-19 households in Hong Kong confirmed positivity in two dogs by molecular and serological assays, with virus being isolated in one case and α have less advantage over the variant. However, there has also been a press report of a dog showing mild respiratory symptoms and testing positive for SARS-CoV-2 in North Carolina, USA, but a cat and another dog from the same COVID-19 household tested negative.

From a Belgian COVID-19 household, a cat showed respiratory and gastrointestinal symptoms and shed the virus in faeces and gastric fluid, but recovered. Two cats from two independent households in New York state also tested positive by reverse transcription—polymerase chain reaction (RT-PCR), one from a COVID-19 household and the other within an affected neighbourhood and allowed to go outdoors, with the latter reportedly showing respiratory symptoms. A cat from Hong Kong also showed positivity without symptoms. Further, 15 (14.7%) of 102 cats tested after the outbreak started in Wuhan were found to carry antibodies to SARS-CoV-2 by enzyme-linked immunosorbent assay (ELISA), and 11 samples showed neutralization of SARS-CoV-2 and no cross-reactivity with feline coronavirus; these samples had been obtained from stray cats, at a veterinary hospital and from animals owned by patients. Thus, it appears that while cats and other felids can be infected, the infection rate may be low, and a symptomatic outcome is rare. In support of this, a study has reported no infection of 9 cats and 12 dogs which were in close contact with COVID-19 patients in a veterinary campus in France.
| Animals | SARS-CoV-2 strain | Dose | Inoculation route | Symptoms | Findings | References |
|---------|------------------|------|------------------|----------|---------|------------|
| HFH4-hACE2 C3B6 mice | SARS-CoV-2 (IVCAS 6.7512) | Primary infection: \(3 \times 10^4\) TCID<sub>50</sub>  
Challenge: \(7 \times 10^5\) TCID<sub>50</sub> | Intranasal | No visible clinical signs up to 3 DPI; respiratory distress and recovery; some show rapid weight loss | Interstitial pneumonia; virus replication in lungs, brain. Some animals showed death with neurological symptoms. Pre-exposure to virus protects mice from high-dose virus challenge | 32 |
| Mice expressing hACE2 by CRISPR/Cas9 knock-in | SARS-CoV-2 strain (BetaCoV/Wuhan/AMMS01/2020) | 4 \(\times\) 10<sup>5</sup> PFU  
4 \(\times\) 10<sup>6</sup> PFU | Intranasal  
Intragastic | Intestinal pneumonia | Virus replication in lungs trachea and brain. Intragastric route led to respiratory tract infection | 33 |
| Transgenic mice expressing hACE2 | SARS-CoV-2 strain HB-01 | 10<sup>5</sup> TCID<sub>50</sub> | Intranasal | Weight loss | Virus replication in lungs, interstitial pneumonia and infiltration of macrophages and lymphocytes | 28 |
| Mice (BALB/c) | SARS-CoV-2 MA10 (SARS-CoV-2 MA passaged ten times in mice to obtain) | 10<sup>2</sup>, 10<sup>3</sup>, 10<sup>4</sup> and 10<sup>5</sup> PFU | Intranasal | Dose-dependent increase in morbidity and mortality | Mortality rates of 20% for 10<sup>4</sup> PFU dose and 60% for 10<sup>5</sup> PFU dose | 27 |
| Mice (BALB/c) | SARS-CoV-2 MA (Recombinant SARS-CoV-2 with designed spike for mouse adaptation) | 10<sup>5</sup> PFU | Intranasal | Mild to moderate disease | Virus replication high in lung tissue on 2 DPI but was cleared by 4 DPI | 29 |
| Mice transduced with adeno-associated virus 9 encoding hACE2 (5 \(\times\) 10<sup>9</sup> genomic copies/animal, intratracheal) | SARS-CoV-2 isolate USA-WA1/2020 | 10<sup>6</sup> PFU | Intranasal | – | No significant difference between viral RNA or viral titre between IFN-α receptor-deficient B6/J mice, IFN regulatory factor 3/7 double knockout B6/J, and wild type B6/J AAV-hACE2-infected mice. Antibody response observed between 4 and 7 DPI which increased till 14 DPI | 36 |
| BALB/c Mice transduced with adenovirus 5 expressing hACE2 (2.5 \(\times\) 10<sup>6</sup> PFU/animal, intranasally) | SARS-CoV-2 strain 2019 n-CoV/USA_WA1/2020 | 10<sup>5</sup> Focus Forming Unit | Intranasal or Intranasal and intravenous | Weight loss | High level of viral RNA detected in lung. Viral RNA not detected in kidney, gastrointestinal tract tissues, or in serum | 35 |
| Animals                  | SARS-CoV-2 strain                                                                 | Dose           | Inoculation route | Symptoms                      | Findings                                                                 | References |
|-------------------------|----------------------------------------------------------------------------------|----------------|------------------|-------------------------------|--------------------------------------------------------------------------|------------|
| Mice (HFH4-hACE2)       | SARS-CoV-2                                                                        | $10^5$ PFU     | Intranasal       | –                             | 40% of infected mice died. Virus detected in lungs on 2 and 5 DPI. It was also detected in brain on 5 DPI | 29         |
| Mice (K18-hACE2 mice)   | SARS-CoV-2 (strain 2019n-CoV/USA_WA1/2020)                                      | $2.5 \times 10^4$ PFU | Intranasal       | Weight loss                   | Highly susceptible, succumb to disease by 7 DPI. High levels of virus and viral RNA detected in the lungs | 31         |
| Mice (HFH4-hACE2)       | Recombinant SARS-CoV-2 virus with D614G mutation in spike derived from WA1 strain | $10^3$ PFU     | Intranasal       | Minimum body weight loss       | High viral titres in lungs and brain tissue. Similar susceptibility to wild-type and D614G variant | 30         |
| Syrian Hamster          | SARS-CoV-2 isolated from Honk Kong patient                                       | $10^5$ PFU     | Intranasal       | Weight loss, rapid breathing   | Animal-to-animal transmission demonstrated through direct contact. On 14 DPI, all infected hamsters had neutralizing antibody titres $\geq 1:427$ | 37         |
| Syrian Hamster          | SARS-CoV-2/UT-NCGM02/ Human/2020/Tokyo and SARS-CoV-2/UW-001/ Human/2020/Wisconsin | $10^{5.6}$ or $10^3$ PFU | Intranasal and intraocular | Weight loss                   | High susceptibility                                                      | 38         |
| Syrian Hamster          | Recombinant SARS-CoV-2 virus with D614G mutation in spike derived from WA1 strain | $10^3$ PFU     | Intranasal       | Weight loss                   | High susceptibility for D614G variant with significantly faster spread between hamsters through aerosol and droplets | 30         |
| Mink                    | SARS-CoV-2/HRB25/ human/2020/CHN (HRB25, GISAID access no. EPI_ISL_467430)         | $5 \times 10^6$ PFU | Intranasal       | Weight loss between 10 and 20% at around 8 DPI; 5% in in-contact animals | Highly susceptible. Upper and lower respiratory tract infection. Viral RNA and infectious virus detected in most of the respiratory tract samples, with severe lung pathology. Virus transmission through droplet observed | 39         |
Table 1: (continued)

| Animals | SARS-CoV-2 strain | Dose | Inoculation route | Symptoms | Findings | References |
|----------|-------------------|------|------------------|----------|----------|------------|
| Ferrets  | SARS-CoV-2/F13/environment/2020/Wuhan or SARS-CoV-2/CTan/human/2020/Wuhan | $10^5$ PFU | Intranasal | Fever and loss of appetite | Viral RNA and infectious virus detected in the nasal turbinate, soft palate, and tonsils of infected ferrets. Virus replication in upper respiratory tract up to 8 days without causing severe disease or death | 40 |
| Ferrets  | SARS-CoV-2 isolate from South Korea (NMCnCoV02) | $10^{5.5}$ TCID$_{50}$ | Intranasal | Fever, acute bronchiolitis | Highest infectious virus and viral RNA detected in nasal washes of infected ferrets on 4 DPI. Virus also shed in saliva, urine and faeces. Viral RNA detected in nasal washes and faeces of contact animals. Ferret-to-ferret transmission detected | 41 |
| Ferrets  | SARS-CoV-2 (isolate BetaCoV/Munich/Bav-Pat1/2020) | $6 \times 10^5$ TCID$_{50}$ | Intranasal | Not defined | Ferret-to-ferret transmission demonstrated through direct contact and indirect contact through respiratory droplets. Infectious titre ranged between 0.75 and 2.75 $\log_{10}$ TCID$_{50}$/ml in the donor ferrets, from 0.75 to 3.5 $\log_{10}$ TCID$_{50}$/ml in the direct contact ferrets from 0.75 to 4.25 $\log_{10}$ TCID$_{50}$/ml in the indirect contact ferrets. Infected ferrets in all groups seroconverted by 21 DPI or exposure | 42 |
| Cats     | SARS-CoV-2 isolate UT-NCGM02/Human/2020/Tokyo | $5.2 \times 10^5$ PFU | Combination of intranasal, intratracheal, oral and ocular | -- | Virus detected in all inoculated cats by 3 DPI. Virus detected in co-housed animals by 5 DPI | 44 |
Table 1: (continued)

| Animals       | SARS-CoV-2 strain                  | Dose          | Inoculation route | Symptoms                                                                 | Findings                                                                                     |
|---------------|------------------------------------|---------------|-------------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Cats          | SARS-CoV-2/CTan/human/2020/Wuhan   | 10^5 PFU      | Intranasal        | –                                                                         | Viral RNA detected in nasal turbinates, soft palates, tonsils, trachea, or small intestine. Viral RNA not detected in lungs. Virus detected in the upper respiratory tract, tonsils, tracheas, and lungs but not in the small intestines. Younger cats more susceptible than older cats. Cat-to-cat transmission detected |
| Cats          | SARS-CoV-2 virus strain WA1/2020WY96 | 3 X 10^5 PFU  | Intranasal        | No clinical signs                                                        | Virus shedding up to 5 DPI. Contact cat shed virus up to 7 DPI. Seroconversion by 7 DPI. Neutralizing antibody titres $\geq 1:2560$ by 14 DPI. Virus shedding not detected in challenged cats |
| Rhesus macaques | SARS-CoV-2 isolate nCoV-WA1–2020 | 2 x 10^5 TCID$_{50}$ | Intranasal        | Initial weight loss, irregular respiratory pattern and piloerection, reduced appetite, hunched posture, pale appearance, dehydration | High susceptibility. Virus shedding highest in nose, throat and bronchioalveolar lavage (BAL). Virus isolated from nose and BAL on 1 and 3 DPI. Pulmonary infiltrates visible in lung radiographs |
| Rhesus macaques | SARS-CoV-2/WH09/human/2020/CHN | 2 x 10^5 TCID$_{50}$ | Intranasal        | Interstitial pneumonia and systemic viral dissemination mainly in the respiratory and gastrointestinal tracts | Initial infection with SARS-CoV-2 protects against reinfection during early recovery phase. Reinfection increased neutralizing antibodies |
| Rhesus macaques | SARS-CoV-2 USA-WA1/2020 | Primary infection: 1.1 x 10^4 or 1.1 x 10^5 or 1.1 x 10^6 PFU | Intranasal and Intratracheal | Intestinal pneumonia                                                      | High viral loads in the upper and lower respiratory tract. Primary infection with SARS-CoV-2 protects against rechallenge on 35 DPI. Up on reinfection, median viral load reduced by 5 log$_{10}$ in BAL and nasal mucosa |
Table 1: (continued)

| Animals       | SARS-CoV-2 strain                      | Dose                  | Inoculation route              | Symptoms                                      | Findings                                                                 | References |
|---------------|----------------------------------------|-----------------------|--------------------------------|-----------------------------------------------|--------------------------------------------------------------------------|------------|
| Rhesus macaques | SARS-CoV-2 USA-WA1/2020                 | $1.05 \times 10^6$ PFU | Ocular, intratracheal and intranasal | Acute respiratory distress. Mild-to-moderate pneumonia | Old and young age groups recover in two weeks. T cell memory and bystander cytokine production. Lower titres of specific IgG antibodies in old animals | 49         |
| Cynomolgus macaques | SARS-CoV-2 (isolate BetaCoV/Munich/Bav-Pat1/2020) | $10^6$ TCID$_{50}$ | Intranasal and Intratracheal | No clinical sign | Virus shedding from nose and throat. SARS-CoV-2 antigen detected in type I and II pneumocytes in affected lung and in ciliated epithelial cells of nasal, bronchial, and bronchiolar mucosae | 50         |
| Baboons       | SARS-CoV-2 USA-WA1/2020                 | $1.05 \times 10^6$ PFU | Ocular, intratracheal and intranasal | Acute respiratory distress, severe pneumonia | Infectious virus detected on 3 DPI. Highest viral load in rectal swab | 49         |
| Marmosets     | SARS-CoV-2 USA-WA1/2020                 | $1.05 \times 10^6$ PFU | Ocular, intratracheal and intranasal | Mild infection | Viral RNA peaked at 3 DPI | 49         |
| White-tailed deer | SARS-CoV-2 TGR/NY/20 (isolated from infected tiger) | $5 \times 10^6$ TCID$_{50}$ | Intranasal | Subclinical infection | Virus shedding detected in nasal secretions from all inoculated and contact animals | 51         |
| White-tailed deer | SARS-CoV-2/humanUSA/ WA1/2020 lineage A | 2 ml dose of $1 \times 10^6$ TCID$_{50}$ per animal (1:1 titre ratio of both viruses) | Intranasal and oral | Subclinical infection | Virus shedding through nasal and oral secretions of infected animals and contact animals. B.1.1.7 isolate sequence more than the lineage A WA1 isolate sequence. Virus transmission through direct contact and vertically from doe to foetus | 52         |
| Sheep         | SARS-CoV-2/humanUSA/ WA1/2020 lineage A | 2 ml dose of $1 \times 10^6$ TCID$_{50}$ per animal (1:10 titre ratio of lineage A: lineage B) | Intranasal and oral | Mild infection | Oral and nasal swab positive on 1 DPI. Viral RNA detected in respiratory tract and lymphoid tissues at 4 and 8 DPI. Virus transmission to naïve animals were limited | 53         |
Table 1: (continued)

| Animals          | SARS-CoV-2 strain                  | Dose            | Inoculation route | Symptoms                        | Findings                                                                 | References |
|------------------|-----------------------------------|-----------------|-------------------|---------------------------------|---------------------------------------------------------------------------|------------|
| Dogs             | SARS-CoV-2 virus strain WA1/2020WY96 | $1.4 \times 10^5$ PFU | Intranasal        | No clinical signs                | Virus shedding not detected. Neutralizing antibody titres between 1:40 and 1:80 at 14 to 21 DPI | 45         |
| Dogs             | SARS-CoV-2/CTan/human/2020/Wuhan   | $10^5$ PFU      | Intranasal        | No clinical signs                | Low susceptibility. 2 out of 4 dogs seroconverted. Dog-to-dog transmission not detected | 40         |
| Racoon dogs      | SARS-CoV-2 2019_nCoV Muc-IMB-1     | $10^5$ TCID$_{50}$ | Intranasal        | No clinical signs                | Virus detected in nasal and oropharyngeal swab samples on days 2–4. 66.6% of the contact animals infected | 43         |
| Cattle           | SARS-CoV-2 strain Muc-IMB-1        | $10^5$ TCID$_{50}$ | Intranasal        | No clinical signs                | Virus replication and seroconversion in 2 or 6 animals. Cattle-to-cattle transmission not detected | 47         |
| Tree shrews      | SARS-CoV-2 (strain not defined)    | $10^6$ PFU      | Intranasal        | Fever in young and old than adult animals | Low susceptibility. Highest viral load in pancreas in one animal | 48         |
| Bank voles       | SARS-CoV-2 strain Muc-IMB-1        | $10^5$ TCID$_{50}$ | Intranasal        | No clinical signs                | Seroconversion within 8 days and viral RNA detected in nasal tissue for up to 21 days. Transmission to contact animals not detected | 46         |
| Pigs, chickens and ducks | SARS-CoV-2/CTan/human/2020/Wuhan | $10^5$ PFU      | Intranasal        | No clinical signs                | Not susceptible                                                           | 40         |

*DPI* days post-infection, *PFU* plaque-forming units, *TCID$_{50}$* 50% tissue culture infective dose
Table 2: Natural infection of SARS-CoV-2 in animals.

| Species       | Number | Country                        | Month and year                  | References                                                                 |
|---------------|--------|-------------------------------|---------------------------------|---------------------------------------------------------------------------|
| Pet animals   |        |                               |                                 |                                                                           |
| Dog           | 2      | Hong Kong                     | February to March 2020          |                                                                           |
|               | 1      | Netherlands                   | April 2020                      | https://www.rijksoverheid.nl/documenten/kamerstukken/2020/05/15/kamerbrief-over-corona-bijdieren |
|               | 18     | USA                           | June to July 2020               | https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf |
|               | 1      | Denmark                       | June 2020                       | https://www.oie.int/fileadmin/Home/MM/Update_1_Letter_to_OIE_about_the_COVID-19_situation_in_Denmark.pdf |
|               | 2      | Hong Kong                     | July to Sept 2020               | https://wahis.oie.int/#/report-info?reportId=15464                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=15471                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=15620                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=15702                     |
|               | 4      | Japan                         | July 2020 to November 2020     | https://wahis.oie.int/#/report-info?reportId=16168                     |
|               | 12     | USA                           | August to September 2020       | https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf |
|               | 10     | Mexico                        | August 2020 to March 2021      | https://wahis.oie.int/#/report-info?reportId=16869                     |
|               | 1      | Canada                        | October 2021                    | https://www.oie.int/fileadmin/Home/MM/CFIA_ACIA_14346824-v3-OIE_SARS-CoV-2_in_dog_letter_002_.pdf |
|               | 4      | Argentina                     | October 2021                    | https://wahis.oie.int/#/report-info?reportId=25035                     |
|               | 18     | Brazil                        | October 2020 to March 2021     | https://wahis.oie.int/#/report-info?reportId=16113                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=16847                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=31367                     |
|               | 6      | Hong Kong                     | November 2020 to January 2021  | https://wahis.oie.int/#/report-info?reportId=16336                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=16423                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=16464                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=16524                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=16700                     |
|               |        |                               |                                 | https://wahis.oie.int/#/report-info?reportId=16939                     |
|               | 2      | Germany                       | November 2020                  | https://wahis.oie.int/#/report-info?reportId=16869                     |
|               | 1      | Hong Kong                     | January to February 2021       | https://wahis.oie.int/#/report-info?reportId=17017                     |
|               | 1      | Bosnia and Herzegovina        | February 2021                  | https://wahis.oie.int/#/report-info?reportId=28184                     |
|               | 17     | USA                           | October 2020 to November 2021  | https://wahis.oie.int/#/report-info?reportId=42300                     |
|               | 4      | Argentina                     | March 2021                     | https://wahis.oie.int/#/report-info?reportId=30744                     |
|               | 2      | Croatia                       | April 2021                     | https://wahis.oie.int/#/report-info?reportId=32538                     |
|               | 1      | Switzerland                   | April 2021                     | https://wahis.oie.int/#/report-info?reportId=35662                     |
|               | 1      | Thailand                      | May 2021                       | https://wahis.oie.int/#/report-info?reportId=33320                     |
|               | 1      | Uruguay                       | May 2021                       | https://wahis.oie.int/#/report-info?reportId=33930                     |
|               | 2      | Brazil                        | May 2021                       | https://wahis.oie.int/#/report-info?reportId=34358                     |
|               | 1      | Japan                         | May 2021                       | https://wahis.oie.int/#/report-info?reportId=34040                     |
|               | 4      | Croatia                       | June to November 2021           | https://wahis.oie.int/#/report-info?reportId=34882                     |
|               | 1      | Switzerland                   | July 2021                      | https://wahis.oie.int/#/report-info?reportId=38903                     |
| Species | Number | Country | Month and year | References |
|---------|--------|---------|----------------|------------|
| Cat     | 1      | Myanmar| October 2021   | [link](https://wahis.oie.int/#/report-info?reportId=40712) |
|         | 1      | Belgium | March 2020     | [link](https://wahis.oie.int/#/report-info?reportId=40968) |
|         | 1      | Hong Kong| March 2020    | [link](https://wahis.oie.int/#/report-info?reportId=14982) |
|         | 1      | China   | April 2020     | [link](https://wahis.oie.int/#/report-info?reportId=14765) |
|         | 1      | Spain   | April 2020     | [link](https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf) |
|         | 2      | USA     | April 2020     | [link](https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf) |
|         | 2      | France  | May 2020       | [link](https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf) |
|         | 1      | Germany | May 2020       | [link](https://wahis.oie.int/#/report-info?reportId=15477) |
|         | 1      | Spain   | May 2020       | [link](https://wahis.oie.int/#/report-info?reportId=15471) |
|         | 3      | Netherlands | May 2020   | [link](https://wahis.oie.int/#/report-info?reportId=15702) |
|         | 1      | Russia  | May 2020       | [link](https://wahis.oie.int/#/report-info?reportId=15702) |
|         | 3      | Chile   | June 2020      | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|          | 40     | USA     | June to September 2020 | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 1      | UK      | July 2020      | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 5      | Hong Kong| July–September 2020 | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 2      | Japan   | July 2020 to November 2021 | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 2      | Argentina| October 2020  | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 12     | Brazil  | October 2020 to March 2021 | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 2      | Hong Kong| November 2020 to January 2021 | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 1      | Canada  | November 2020  | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
|         | 2      | Germany | November 2020  | [link](https://wahis.oie.int/#/report-info?reportId=16186) |
| Species     | Number | Country      | Month and year | References                                                                 |
|-------------|--------|--------------|----------------|-----------------------------------------------------------------------------|
| Ferret      | 1      | Slovenia     | December 2020  | https://wahis.oie.int/#/report-info?reportId=28156                        |

**Captive zoo animals**

|          |        |              |                |                                                                            |
|----------|--------|--------------|----------------|---------------------------------------------------------------------------|
| Lions    |        |              |                |                                                                            |
| 3        | USA    | March–April 2020 | 11 | https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf |
| 4        | Spain  | November 2020 |                | https://www.oie.int/fileadmin/Home/MM/Spain_lions_21.12.2020.pdf          |
| 5        | Sweden | January 2021 |                | https://www.oie.int/fileadmin/Home/MM/Sweden_25.01.2021_lion_tiger.pdf    |
| 1        | Estonia| January 2021 |                | https://www.oie.int/fileadmin/Home/MM/Estonia_22.01.2021_Lion.pdf         |
| 17       | India  | June 2021   |                | https://www.dailymail.co.uk/news/article-9540377/ Eight-LIONS-test-positive-Covid-19-Indian-zoo-eight-tested-positive.html |
| 19       | USA    | October 2020 to November 2021 | | https://wahis.oie.int/#/report-info?reportId=42300                      |
| 3        | South Africa | July 2021 |                | https://wahis.oie.int/#/report-info?reportId=36771                       |
| 5        | Singapore | November 2021 |                | https://wahis.oie.int/#/report-info?reportId=42534                      |
| Tiger    |        |              |                |                                                                            |
| 4        | USA    | March–April 2020 | 11 | https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf |
| 1        | Sweden | January 2021 |                | https://www.oie.int/fileadmin/Home/MM/Sweden_15.01.2021_tiger_zoo.pdf    |
| 19       | USA    | October 2020 to November 2021 | | https://wahis.oie.int/#/report-info?reportId=42300                      |
| 2        | Indonesia | September 2021 |                | https://wahis.oie.int/#/report-info?reportId=39313                      |
| Species                        | Number | Country     | Month and year                      | References                                                                 |
|-------------------------------|--------|-------------|-------------------------------------|-----------------------------------------------------------------------------|
| Puma/Cougar                   | 1      | South Africa| July 2020                           | https://wahis.oie.int/#/report-info?reportId=15584                          |
|                               | 1      | USA         | October 2020 to November 2021       | https://wahis.oie.int/#/report-info?reportId=42300                          |
|                               | 1      | Argentina   | February 2021                       | https://wahis.oie.int/#/report-info?reportId=25065                          |
| Snow Leopard                  | 3      | USA         | December 2020                       | https://www.aphis.usda.gov/aphis/newsroom/indicatorinformation/SA_by_date/SA-2020/SA-12/ky-snow-leopard-covid |
|                               |        |             |                                     | https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf |
| Gorillas                      | 10     | USA         | October 2020 to November 2021       | https://wahis.oie.int/#/report-info?reportId=42300                          |
| Coatiundi                     | 1      | USA         | October 2021                        | https://wahis.oie.int/#/report-info?reportId=41500                          |
| Fishing cat                   | 1      | USA         | October 2021                        | https://wahis.oie.int/#/report-info?reportId=41500                          |
| Binturong                     | 1      | USA         | October 2021                        | https://wahis.oie.int/#/report-info?reportId=41500                          |
| Asian small-clawed otter      | 7      | USA         | October 2020 to November 2021       | https://wahis.oie.int/#/report-info?reportId=42300                          |
| Spotted Hyena                 | 2      | USA         | November 2021                       | https://wahis.oie.int/#/report-info?reportId=42300                          |
| Captive farm animals          |        |             |                                     |                                                                             |
| Mink                          | 69     | Netherlands | April 2020 to January 2021          | https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/COVID-19/OIE_SARS_CoV%202_infection_of_mink_in_the_Netherlands_26April2020.pdf |
|                               | 290    | Denmark     | June 2020 to December 2020          | https://old.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/COVID-19/Denmark_Sars-CoV-2_17-06-2020.pdf |
|                               |        |             |                                     | https://old.oie.int/fileadmin/Home/MM/Update_1_Letter_to_OIE_about_the_COVID-19_situation_in_Denmark.pdf |
|                               |        |             |                                     | https://old.oie.int/fileadmin/Home/MM/Update_3_Letter_to_OIE_about_the_COVID-19_situation_in_Denmark.pdf |
|                               |        |             |                                     | https://old.oie.int/fileadmin/Home/MM/Update_4_Letter_to_OIE_on_Sars-CoV-2_in_mink_farms_in_Denmark.pdf |
|                               |        |             |                                     | https://old.oie.int/fileadmin/Home/MM/Update_5_Letter_to_OIE_on_Sars-CoV-2_in_Denmark.pdf |
|                               |        |             |                                     | https://old.oie.int/fileadmin/Home/MM/Update_6_Letter_to_the_OIE_on_Sars-CoV-2_in_Denmark_5_November2020.pdf |
|                               | 2      | Spain       | December 2020 to January 2021       | https://www.oie.int/fileadmin/Home/MM/Informes_OIE_16.07.20_.pdf |
|                               | 16     | USA         | August to November 2020             | https://wahis.oie.int/#/report-info?reportId=16924                           |
|                               | 13     | Sweden      | October to December 2020            | https://www.oie.int/fileadmin/Home/MM/Sweden_Update_1_29.10.2020.pdf        |
|                               |        |             |                                     | https://www.oie.int/fileadmin/Home/MM/Sweden_mink_6Nov2020.pdf              |
|                               |        |             |                                     | https://www.oie.int/fileadmin/Home/MM/Sweden_1_12.2020.pdf                  |
Table 2: (continued)

| Species          | Number | Country   | Month and year         | References                                                                 | References                                                                 |
|------------------|--------|-----------|------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------------------|
|                  | 1 farm | Italy     | October 2020           | https://www.oie.int/fileadmin/Home/MM/Italy_COVID_30.10.2020.pdf           |                                                                            |
|                  |        |           |                        | https://www.oie.int/fileadmin/Home/MM/Italy_mink_11_11_2020-DGSAF-MDS-Pdf  |                                                                            |
|                  |        |           |                        | https://www.oie.int/fileadmin/Home/MM/Ordinanza_21_novembre_2020.pdf       |                                                                            |
|                  | 11 farms | Greece    | December 2020 to February 2021 | https://wahis.oie.int/#/report-info?repid=17059                          | https://wahis.oie.int/#/report-info?repid=17127                          |
|                  | 4 farms | France    | November 2020          | https://wahis.oie.int/#/report-info?repid=16335                          | https://wahis.oie.int/#/report-info?repid=16701                          |
|                  | 4 farm  | Lithuania | November 2020 to March 2021 | https://wahis.oie.int/#/report-info?repid=16373                          | https://wahis.oie.int/#/report-info?repid=16666                          |
|                  | 2 farm  | Canada    | November to December 2020 | https://wahis.oie.int/#/report-info?repid=25040                          | https://wahis.oie.int/#/report-info?repid=25045                          |
|                  | 1 farm  | Poland    | February 2021          | https://wahis.oie.int/#/report-info?repid=31188                          |                                                                            |
|                  | 1 farm  | Spain     | March 2021             | https://wahis.oie.int/#/report-info?repid=32647                          |                                                                            |
|                  | 1 farm  | Italy     | April 2021             | https://wahis.oie.int/#/report-info?repid=32262                          |                                                                            |
|                  | 1 farm  | Latvia    | April 2021             | https://wahis.oie.int/#/report-info?repid=31188                          |                                                                            |
|                  | 1 farm  | Canada    | May 2021               | https://wahis.oie.int/#/report-info?repid=35110                          | https://wahis.oie.int/#/report-info?repid=34464                          |
|                  | 10 farm | Spain     | June to October 2021   | https://wahis.oie.int/#/report-info?repid=35110                          | https://wahis.oie.int/#/report-info?repid=35310                          |
|                  |        |           |                        | https://wahis.oie.int/#/report-info?repid=35311                          | https://wahis.oie.int/#/report-info?repid=35311                          |
|                  |        |           |                        | https://wahis.oie.int/#/report-info?repid=35314                          | https://wahis.oie.int/#/report-info?repid=35655                          |
|                  |        |           |                        | https://wahis.oie.int/#/report-info?repid=36329                          | https://wahis.oie.int/#/report-info?repid=36331                          |
|                  |        |           |                        | https://wahis.oie.int/#/report-info?repid=36331                          | https://wahis.oie.int/#/report-info?repid=37890                          |
|                  |        |           |                        | https://wahis.oie.int/#/report-info?repid=39636                          | https://wahis.oie.int/#/report-info?repid=40677                          |
|                  |        |           |                        | https://wahis.oie.int/#/report-info?repid=41492                          | https://wahis.oie.int/#/report-info?repid=41617                          |
|                  | 1 farm  | Poland    | June 2021              | https://wahis.oie.int/#/report-info?repid=35103                          |                                                                            |
|                  | 2 farm  | Greece    | August to September 2021 | https://wahis.oie.int/#/report-info?repid=38527                          | https://wahis.oie.int/#/report-info?repid=39710                          |
|                  | 1 farm  | Sweden    | August 2021            | https://wahis.oie.int/#/report-info?repid=38730                          | https://wahis.oie.int/#/report-info?repid=41009                          |
| Beavers          | 1 farm  | Mongolia  | September 2021         | https://promedmail.org/promed-post/?id=8664608                           |                                                                            |
| Wild animals     |        |           |                        |                                                                            |                                                                            |
| White-tailed deer| 8      | USA       | August 2021            | https://wahis.oie.int/#/report-info?repid=38714                          |                                                                            |
| Mink (free-ranging) | 1   | USA       | August to October 2020 | https://www.reuters.com/article/us-health-coronavirus-usa-mink-idUSKBN28O2UR  |                                                                            |

Adapted from https://www.avma.org/resources-tools/animal-health-and-welfare/covid-19/depth-summary-reports-naturally-acquired-sars-cov-2 and updated with the latest information available from various sources.
and only one asymptomatic (but positive by RT-PCR) cat among 12 dogs, 8 cats, 2 rabbits and one guinea pig from 17 confirmed COVID-19 households in Spain. In addition, a serological survey of preserved sera from 487 dogs and 87 cats from among 1914 samples from 35 species of animals from China showed no positivity, although the samples probably predated COVID-19. Studies on pets which belong to COVID-19 patients in Brazil also indicated that the pet animals were susceptible to SARS-CoV-2 infection. Nine out of 29 dogs and four out of 10 cats were seropositive for SARS-CoV-2. Partial genome sequence of SARS-CoV-2 was obtained from the samples, but no virus isolation was attempted. In most of the documented cases of SARS-CoV-2 infection in dogs and cats, the symptoms were variable; while most of the animals were asymptomatic, some of the animals had mild respiratory distress. Recent studies have also linked myocarditis as one possible outcome with SARS-CoV-2 B.1.1.7 variant infection of dogs and cats.

Direct or indirect evidence of SARS-CoV-2 infection in pet animals during the COVID-19 pandemic exists from Germany, Italy, Peru, the USA, France and several other countries. In multiple cases, genome sequences of SARS-CoV-2 obtained from pet animals were similar to that of the circulating human strains. For example, the SARS-CoV-2 genome sequence from a cat had D614G mutation specific to the phylogenetic clade A2 observed in the French SARS-CoV-2 genome sequences. Studies in France also showed that the SARS-CoV-2 genome sequences from a pet dog and its COVID-19 affected owners were of B.1.160 lineage with 99–100% identity. The SARS-CoV-2 genome from a domestic cat was close to the human B.1.1.39 lineage in Switzerland. Similar observations have been made in Argentina, where the SARS-CoV-2 genome sequence from domestic cats belonged to the B.1.499 lineage, which circulated in humans in that region. In one instance, the SARS-CoV-2 genome sequence of the owner and the pet animals (dog and cat) from the same household were found to be identical and belonged to the B.1.575 lineage.

In a seroprevalence study on samples collected from cats (2160 samples) from Germany, the UK, Italy and Spain, 96 samples (4.4%) were positive by virus neutralization test and 92 samples (4.3%) were positive by an ELISA for the RBD. Apart from pet animals, SARS-CoV-2 can also infect captive and farm animals. Mild respiratory symptoms were reported in five tigers and three lions in the Bronx zoo, New York, supposedly from being in contact with a COVID-19 asymptomatic zookeeper; SARS-CoV-2 was confirmed by RT-PCR, the virus was isolated, and complete viral genome sequence was elucidated in the case of a Malayan tiger. Virus isolation was not attempted from other zoo animals. Interestingly, SARS-CoV-2 genome sequence from tigers and lions was of different genotypes, which indicates two independent sources of infection.

Other zoo and captive animals that can be infected include puma, mink (farmed and wild), lion, tiger, ferret, snow leopard, gorilla, otter, cougar, coati, binturong, Canadian lynx and hyena. While most of the animals showed mild symptoms of cough and respiratory distress with or without nasal discharge and recovered later, four snow leopards succumbed to SARS-CoV-2 infection at the Great Plains Zoo, South Dakota, USA.

Fur industry across various countries has been affected severely due to the high susceptibility of minks to SARS-CoV-2. Netherlands reported the first outbreak of SARS-CoV-2 in a mink farm in April 2020. Since then, the disease has been reported from Denmark, the USA, France, Greece, Italy, Poland, Lithuania, Canada, Spain and Sweden. Minks are housed in confined spaces, and the infection could spread rapidly among them through droplets. Severity of respiratory sickness is pronounced in minks with high mortality and post-mortem findings of acute interstitial pneumonia. Considering the severity of the disease, Denmark, Spain, the Netherlands and France culled entire affected mink colonies and the Netherlands has banned mink farming permanently.

In the Netherlands, one mink farm worker was found positive for the virus and clear evidence of mink-to-mink transmission was established. Three out of 11 tested cats in one of the farms were also positive for anti-SARS-CoV-2
antibodies, but no viable virus could be detected, although the direction of transmission is not clear in this case. In one of the outbreaks, a probable mink-to-feral cat transmission was recorded. Mink-to-human transmission was also established based on the sequence data from the Netherlands, Denmark and the USA. SARS-CoV-2 virus isolates obtained from minks with Spike Y453F/D614G mutation have higher affinity to hACE2. Whole-genome sequencing of the SARS-CoV-2 from minks revealed 170 mutations, and the mink-specific mutations of SARS-CoV-2 were also found in 300 samples collected from humans indicating mink-to-human transmission. By contrast, the mink SARS-CoV-2 genome from Greece lacked the Y453F mutation in the S protein, suggesting differential adaptability or simply randomness in the emergence of the variants.

Recently, transmission of SARS-CoV-2 was recorded from Syrian hamsters to humans in a pet shop at Hong Kong. Further investigation revealed that Syrian hamsters from both pet shop (50%) and warehouse (58%) were positive for SARS-CoV-2 with RT-qPCR which resulted in the culling of about 2000 hamsters across Hong Kong. The SARS-CoV-2 genome sequence from affected humans and Syrian hamsters belonged to the delta variant (AY.127), and analyses pointed to multiple hamster-to-human transmission events. Interestingly, other animals from the pet shop such as dwarf hamsters, rabbits, guinea pigs, chinchillas and mice tested negative for SARS-CoV-2. This incident is the only documented evidence of Syrian hamsters acquiring SARS-CoV-2 infection in natural settings.

About 40% of the serum samples from white-tailed deer collected by the United States Department of Agriculture between January 2020 and March 2021 were positive for SARS-CoV-2 antibodies. Based on the initial finding, further study was initiated to understand the SARS-CoV-2 strains circulating in deer. Retrropharyngeal lymph nodes were collected from white-tailed deer from Iowa between April 2020 and January 2021. Whole-genome sequence of SARS-CoV-2 from white-tailed deer indicated the presence of 12 lineages of SARS-CoV-2, with the predominance of B.1.2 (54.5%), B.1.311 (20%), B.1 (7%) and B.1.234 (6%) lineages. Surprisingly, the B.1.2 lineage was also the most abundant lineage circulating in humans in Iowa during that period, suggesting multiple human-to-deer and deer-to-human transmissions; however, deer-to-human transmission could not be interpreted from this study.

Brazil has reported the presence of SARS-CoV-2 nucleic acid in wild animals such as Giant anteaters, black-tailed marmoset and West Indian manatee. Since these reports were based on random surveillance, the source of infection could not be determined. However, these findings have further widened the list of animals susceptible to SARS-CoV-2 infection.

6 The Veterinary and One Health Perspective

SARS-CoV-2 infection has been confirmed so far in canids (dogs and raccoon dogs), felids (cats, tigers, lions, puma/cougar, lynx and snow leopard), mustelids (ferrets and minks), viverrids (binturongs), procyonids (coatimundis), hyaenids (hyenas), cervids (white-tailed deer, mule deer), cricetids (Syrian hamster), callitrichids (black-tailed marmoset), myrmecophagids (giant anteater), trichechids (West India manatee), castorids (beaver) and primates (gorilla). With such a wide range of hosts available for the virus, it is possible that the virus can mutate, adapt and be transmitted widely. The close similarity of the SARS-CoV-2 genome sequence between humans and pet animals and the higher incidence of SARS-CoV-2 infection in pet animals during the human pandemic strongly suggest that humans can transmit SARS-CoV-2 to closely in-contact pets such as cats and dogs. On the other hand, transmission of SARS-CoV-2 from cats or dogs to humans is yet to be established and needs further investigation. Though there is no documented evidence of transmission of SARS-CoV-2 from animals to humans, except from minks and Syrian hamsters, animal owners and veterinarians must be vigilant while handling animals with respiratory illness to minimize the potential risk of transmission from pets.

One way to mitigate transmission from animals is to vaccinate the animals. In addition, this could also save endangered animals. Since SARS-CoV-2 has broad host range, it may be practically impossible to vaccinate all the animals. However, susceptible pet animals and captive animals that are in close proximity with humans should be vaccinated in order to avoid any animal-to-human transmission of SARS-CoV-2. However, very few vaccines have been tested or are available for use in animals. An aluminium-adjuvanted subunit vaccine based on modified S protein was demonstrated to protect minks from SARS-CoV-2 challenge. Upon challenge, the virus was not detected in any of the organs that were tested in the vaccinated group while high titre of
the virus was detected in all the organs of control animals. Similarly, black-footed ferrets, which are endangered in North America, could produce neutralizing antibodies when immunized with commercially available purified SARS-CoV-2 Spike protein adsorbed to aluminium oxyhydroxide (alhydrogel® 2%). More than 100 captive animals were then vaccinated in a similar way, and the detailed scientific data are awaited.

Early this year, Russia announced the development and testing of an inactivated SARS-CoV-2-based vaccine named Carnivac-Cov for animals. As per the available information, it has been tested in dogs, cats, minks and foxes and found to be safe and immunogenic. In September 2021, the Finnish Breeders’ Association (FIFUR) announced in collaboration with the University of Helsinki the development of Furcovac, a vaccine for minks. However, scientific details of the vaccine are not in the public domain. Currently, zoo animals and minks in the USA are vaccinated with an adjuvanted SARS-CoV-2 trimeric spike protein-based subunit vaccine. Further scientific data are awaited.

Veterinary professionals can not only contribute to control of animal infectious diseases and play a critical role in contributing to the gross domestic product (GDP) of any nation through improving animal health and farmer’s welfare (to quote Mohandas Gandhi, “the greatness of a nation can be judged by the way its animals are treated”), but also are an important cog in the public health system. Along with other disciplines, the veterinary profession has an equal part in approaching zoonotic diseases holistically, and this includes COVID-19.

Indeed, One Health has its beginnings in veterinary medicine. When the cattle plague rinderpest was decimating bovine populations and disrupting the human food supply, Pope Clement XI is reported to have instructed the papal physician Giovanni Lancisi to provide a solution. This led to Lancisi in 1914, followed by Thomas Bates in England, to recommend culling of affected animals and burying their carcasses and implement restrictions in animal movement. The contributions of Rudolf Virchow also cannot be ignored. Son of a butcher by profession, he experimented on the lifecycle of the parasite Trichinella in the pig muscle as well as cysticercosis and tuberculosis in cattle. He stated that “between animal and human medicine, there are no dividing lines, nor should there be,” and coined the word ‘zoonosis.’ In recent times, veterinary public health specialists James Steele and Calvin Schwabe pioneered the holistic approach to infectious disease medicine. The word One Medicine was coined by Calvin Schwabe in the 1970s. As per this concept, both human and veterinary medicine are considered indifferent and contribute to the development of each other. Later, the concept of “One Medicine” was extended to “One Health” through practical application.

International organizations such as the World Organization for Animal Health (WOAH), the Food and Agriculture Organization (FAO), the World Health Organization (WHO) and the One Health Commission have come together to promote “One Health” and its implementation at various levels. In March 2022, the United Nations Environment Programme (UNEP) joined this One Health alliance. As human, animal, plant and environmental health are intricately intertwined, there is need for concerted efforts for cross-sectoral dialogue and cooperation at all levels in order to promote the well-being of humans and animals. Ultimately, we should move towards Planetary Health. However, the risk of zoonosis or their reporting is not uniform worldwide. Tropical, mostly low-to-middle income countries tend to be at greatest risk of zoonoses, and they need to evolve locally feasible solutions, including developing infrastructure, indigenous low cost diagnostics such as lateral flow assays, strengthening of reporting systems and flow of information, improving care systems in the case of disease outbreaks and implementation of preventive measures, including development of locally deployable vaccines and immunization programs.

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Declarations

Conflict of interest
We declare that we have no financial or other conflicts of interest.

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