COMMENTARY

Third update on possible animal sources for human COVID-19

Tanja Opriessnig1,2 | Yao-Wei Huang3

1The Roslin Institute and The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Midlothian, UK
2Department of Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames, IA, USA
3Institute of Preventive Veterinary Medicine, College of Animal Sciences, Zhejiang University, Hangzhou, China

Correspondence: Tanja Opriessnig, The Roslin Institute and The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Midlothian, UK. Email: tanja.opriessnig@roslin.ed.ac.uk, tanjaopr@iastate.edu

Funding informationThis study was funded by Biotechnology and Biological Sciences Research Council (BBSRC) University of Edinburgh, Roslin Institute (Award Number BBS/E/D/20002173 and BBS/E/D/20002174). Scientific research fund for COVID-19 National Natural Science Foundation of China (Award Number 32041003).

Keywords: animal sources, COVID-19, cross-species transmission, SARS-CoV-2

1 INTRODUCTION

Approximately a year ago, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in humans was described for the first time in Wuhan, China. Since, SARS-CoV-2 and its clinical manifestation, known as coronavirus disease 2019 (COVID-19), have dominated the news and varying restrictions to everyday life have been introduced in essentially all continents in an international effort to limit human-to-human spread as well as decrease hospitalization rates. Updated information on confirmed high pathogenic CoV infections and fatalities in humans are provided in Table 1. This synopsis represents the third update on recent findings on animal sources that could pose a risk for human SARS-CoV-2 infection. The information provided is intended to update people working closely with animals on new evidence of cross-species transmission of SARS-CoV-2 from humans.

2 ORIGIN OF SARS-COV-2: WHAT HAVE WE LEARNED SO FAR?

When assessing any new virus, it is essential to identify its origin as this could yield important data which could help in preventing future outbreaks. Further investigations into the origin of SARS-CoV-2 revealed that the virus itself likely originated from a bat sarbecovirus, a virus circulating in horseshoe bats. Horseshoe bats can be found in tropical and temperate regions in Europe, Japan, Asia, and Africa. Divergence dates between SARS-CoV-2 and the bat sarbecovirus reservoir were estimated as 1948 and 1982, suggesting that the lineage which produced SARS-CoV-2 has been circulating unnoticed in bats for decades. Of note, the virus was introduced to humans via spillover or cross-species transmission but details still need to be established. SARS-CoV-2 adapted quickly to its new human host resulting in rapid human-to-human transmission, with a mean reproductive number (R) estimated to be 3.28 (median 2.79), which indicates that an infected person can potentially infect 3 to 4 others.

In theory, it is possible that SARS-CoV-2 in its current form evolved directly from horseshoe bats, but an intermediate host, such as pangolins or another species, is also plausible. SARS-CoV-2 emerged in Wuhan, China during the winter season, perhaps indicating that there was an intermediate host present at that time. As we outlined in our previous commentary, the pangolin has been proposed as the missing link bridging bats and humans in the context of SARS-CoV-2. Pangolins in some cases have developed natural disease associated with SARS-CoV-2 infection, perhaps indicating they may not be a natural reservoir. The current consensus is that more data is needed to conclusively determine the origin of SARS-CoV-2. Identifying intermediate host species capable of supporting SARS-CoV-2 replication is important as this could provide clues on future reservoir hosts. It has been determined that the likelihood of fish, birds, reptiles and amphibians to become a possible SARS-CoV-2 intermediate host in the future is low. Among livestock species including ruminants, pigs...
and domestic poultry, reports of serious disease outbreaks, possibly suggesting a species jump of SARS-CoV-2, have not been reported to date. However, there is evidence that pigs\(^\text{17}\) and ruminants\(^\text{12}\) can be experimentally infected with SARS-CoV-2 at a low level, and livestock may pose a greater risk of serving as a reservoir in the future, when SARS-CoV-2 becomes more established in humans.\(^\text{13}\) A potentially important role in cross-species transmission has been suggested for rodents including squirrels, rats, mice, hamster and others.\(^\text{14}\) Rodents exist in sufficient numbers and densities for continuous transmission and are often in close proximity to humans, but so far experimental studies indicate a low probability or no risk of SARS-CoV-2 infection for mice and rats.\(^\text{13}\) Interestingly, it has been found more recently that Chinese tree shrews, a squirrel-like mammal with a wide distribution in Southeast Asia, could not only be infected with SARS-CoV-2 but also developed clinical signs analogous to COVID-19 in humans.\(^\text{15}\) Chinese tree shrews have been used as animal models in viral hepatitis, psychosocial and visual defect studies due to their phylogenetical closeness to primates.\(^\text{16}\)

3 | Viral Species Jump of SARS-CoV-2 and Implications: Why Is It Important?

Many research efforts focus on the animal-human interface of SARS-CoV-2. With the high rate of infections and the overall high virus load present in the human population today, it is likely that SARS-CoV-2 may enter other new hosts. This process is known as species jump or spillover and requires some level of adaption of the virus to the new host. Three stages of viral disease emergence leading to successful host switching have been defined previously.\(^\text{17}\)

3.1 | Stage 1

During the first stage, a new host species becomes infected but there is no onward transmission. This scenario is likely true for dogs and cats: SARS-CoV-2-viremia or even clinical signs have occasionally been demonstrated in these pets, which were essentially always in close contact with COVID-19 infected humans and were the direct results of human-dog infection\(^\text{18}\) or human-cat-infection.\(^\text{19}\) However, to date, there have been no confirmed natural infections between dogs, between cats or from cats or dogs to humans and companion animals are unlikely to spread COVID-19 at a larger scale.\(^\text{20}\) Of note, naive cats kept under experimental conditions in close contact with SARS-CoV-2 infected cats can become infected, confirming a successful transmission between cats.\(^\text{21,22}\) However, under normal circumstances domesticated cats live solitary lives without socially structured groups and are not in regular close contact with other cats. The documented events so far suggest that pet cats and dogs can be considered dead-end hosts.

3.2 | Stage 2

The second stage of viral disease emergence are spillovers that go on to cause local chains of transmission in the new host population before the epidemic fades out (outbreaks). The authors are not aware of any SARS-CoV-2 infections in domestic or wild animals that fall into this category.

3.3 | Stage 3

The third stage is development of an epidemic or sustained endemic host-to-host disease transmission in the new host population. This stage has likely been reached in farmed mink populations, where all factors consistent with stage three have been observed, including confirmed human-to mink infections, mink-to-mink transmission with clinical signs in a large number of animals and mink-to-human infection.\(^\text{23}\) This has resulted in the culling of many commercial mink farms in the Netherlands,\(^\text{24}\) Spain (https://www.bbc.co.uk/news/world-europe-53439263), the USA (https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/sa_by_date/sa-2020/sa-08/sarcov-2-mink) and Denmark\(^\text{25}\) among other countries.

The species jump of viruses into a new host is in general of concern because of the potential introduction of genome mutations driven by inadequate replication in the intermediate or novel host. These changes can impact virus fitness in general and occasionally may result in increasing viral replication rate in the intermediate or novel host.\(^\text{26}\) Unique SARS-CoV-2 mutations were identified in Dutch and also in Danish mink after the virus adapted to this species.\(^\text{25,27}\) Subsequently, the same mutated viruses were also detected in humans who were in close contact with

### Table 1 Facts on high pathogenic human CoVs

| Virus         | Time of circulation | Laboratory confirmed cases | Deaths | Case fatality rate | Country distribution |
|---------------|---------------------|-----------------------------|--------|-------------------|-----------------------|
| SARS-CoV\(^a\) | 2002-2003           | 8096                        | 774    | 9.6%              | 26                    |
| MERS-CoV\(^b\) | 2012-ongoing        | 2494                        | 853    | 35%               | 27                    |
| SARS-CoV-2\(^c\) | 2019-ongoing        | 67,210,778                  | 1,540,777 | 2.3%            | Global pandemic       |

\(^a\)Source: https://www.who.int/csr/sars/country/table2004_04_21/en/.

\(^b\)Source: https://www.who.int/emergencies/mers-cov/en/.

\(^c\)Source: https://covid19.who.int (Accessed 9 Dec 2020).
the mink. During vaccine development, it is crucial to monitor any viral changes which may occur at vaccine target sites, as these may render a novel vaccination product ineffective. At this point, scientists suggest that the mink-specific SARS-CoV-2 mutations identified so far will not jeopardize the effectiveness of potential COVID-19 vaccines.

SARS-CoV-2 belongs to the RNA class of viruses, which are prone to high mutation rates (expressed as the number of substitutions per nucleotide per generation). Despite this fact, fortunately and similar to SARS-CoV, which is mutating at a slow rate \(0.80-2.38 \times 10^{-3}\) nucleotide substitution/site/year, SARS-CoV-2 has an estimated annual substitution rate of \(26\) and an estimated evolutionary rate of approximately \(0.90 \times 10^{-5}\) substitution/site/year. In lay terms, this means that SARS-CoV-2 only has approximately two single mutations per month on average; this is half the rate seen in influenza viruses and a quarter of the mutations acquired by HIV.

4 | NEW INFORMATION ON SARS-COV-2 SUSCEPTIBLE ANIMAL SPECIES

At the time of our last update, it had been confirmed that Felidae, Canidae, and Mustelidae can become naturally infected with SARS-CoV-2. Under experimental conditions, Cricetidae and Macaques can also be infected but often only develop subclinical disease. The following information is an update on the current knowledge relevant to the susceptibility of different animal groups to SARS-CoV-2.

4.1 | SARS-CoV-2 in pets

Today pets often live in close contact with humans and are commonly considered part of the family. It comes as no surprise that SARS-CoV-2 has been detected in dogs and cats living in COVID-19 households. Often SARS-CoV-2 in cats or dogs was only detected by PCR assays, occasionally the pet in question seroconverted, and in only a few cases, mild clinical signs were described.

Commonly, field assessments of the general cat and dog population using serology assays resulted in a low prevalence of antibody-positive animals. Overall, this has triggered a number of controlled experimental and observational studies. Since our last update, a few more experimental cat studies have been published (Table 2) further confirming that cats often remain asymptomatic while able to transmit SARS-CoV-2 to sentinel cats. Moreover, it was also reported that cats shed the virus for approximately 5 days with peak titres achieved from nasal shedding at day 3 and, when infected with SARS-CoV-2 twice 4 weeks apart, mounted an effective immune response and did not become reinfected. In contrast, SARS-CoV-2 shedding in experimentally infected dogs was not observed; however, seroconversion was reported. The overall data provided by research into canine and feline SARS-CoV-2 infection indicates these are end-stage hosts, there is no evidence of virus transmission to other dogs, but cats can infect naïve cats during the acute stage of infection if in close contact with each other.

Under experimental conditions, Golden Syrian hamsters as well as ferrets can be readily infected with SARS-CoV-2, which causes mild to no clinical signs with limited and often short-lived

| TABLE 2 | Summary of research studies demonstrating SARS-CoV-2 in pets |
| Species | Data type | Positive animals/total number of animals tested | Inoculation details | Reference |
| --- | --- | --- | --- | --- |
| Domestic cats | Experimental | 14/14 | Intranasal | 1.0 × 10^5 PFU | 43 |
| | | 6/6 | Oral/intranasal | 1.0 × 10^6 TCID<sub>50</sub> | 38 |
| | | 6/6 | Intranasal/oral | 5.2 × 10^5 PFU | 21 |
| | | 5/5 | Intranasal | 3.0 × 10^5 PFU | 22 |
| | Surveillance | 6/60 | NA<sup>a</sup> | NA | 44 |
| | | 0/87 | NA | NA | 45 |
| | | 1/131 | NA | NA | 36 |
| | | 15/39 | NA | NA | 37 |
| Domestic dogs | Experimental | 1/5 | Intranasal | 1.0 × 10^5 PFU | 43 |
| | | 3/3 | Intranasal | 1.4 × 10^5 PFU | 22 |
| | Surveillance | 8/180 | NA | NA | 44 |
| | | 0/497 | NA | NA | 45 |
| | | 13/172 | NA | NA | 36 |
| Ferrets | Experimental | 10/10 | Intranasal | 1.0 × 10^5 TCID<sub>50</sub> | 46 |
| | | 9/9 | Intranasal | 1.0 × 10^5 PFU | 43 |

<sup>a</sup>Median tissue culture infectious dose (TCID<sub>50</sub>) per animal or plaque-forming unit (PFU).

<sup>b</sup>NA, not available.
virus shedding. To the authors’ knowledge, there have been no reports of SARS-CoV-2 naturally infecting pet hamsters or ferrets.

In general, it would appear pets are not easily infected. Confirmed reports of cats and dogs naturally infected with SARS-CoV-2 are very limited, while confirmed human infections have reached over 67 million cases, as outlined in Table 1. Therefore, pets do not pose a major threat to humans at this point and human infection from cats, dogs, ferrets or Golden Syrian hamsters has not been reported.

### 4.2 SARS-CoV-2 in livestock species

Fortunately, studies investigating the susceptibility of livestock species to SARS-CoV-2 have rarely resulted in finding viral infectivity (Table 3). SARS-CoV-2 experimental infection trials in poultry using chickens, ducks, turkeys, quail and geese demonstrated these animals lacked susceptibility to the virus.46,47

---

**TABLE 3** Summary of research into SARS-CoV-2 infection in livestock species

| Species   | Data type   | Positive animals/total number of animals tested | Route            | Dosea                           | Reference |
|-----------|-------------|------------------------------------------------|-------------------|---------------------------------|-----------|
| Pigs      | Experimental| 0/9                                             | Intranasal        | $1 \times 10^5 \text{TCID}_{50}$ | 46        |
|           |             | 0/5                                             | Intranasal        | $1 \times 10^5 \text{PFU}$     | 43        |
|           |             | 0/9                                             | Oral/intranasal/intratracheal | $1 \times 10^6 \text{TCID}_{50}$ | 48        |
|           |             | 0/20                                            | Intranasal, intratracheal, intramuscular or intravenous | $1 \times 10^{5.8} \text{TCID}_{50}$ | 49        |
|           | Surveillance| 3/16                                            | Oronasal          | $1 \times 10^6 \text{PFU}$     | 11        |
|           |             | 0/187                                           | NAa               | NA                             | 45        |
|           | Swine cell lines | Infection readily possible | Swine testicle (ST) cell line | 0.05 multiplicity of infection (MOI) of passage 3 of a VeroE6-passaged SARS-CoV-2 | 48        |
| Cattle    | Experimental| 2/6                                             | Intranasal        | $1 \times 10^5 \text{TCID}_{50}$ | 12        |
|           | Surveillance| 0/107                                           | NA                | NA                             | 45        |
| Sheep     | Surveillance| 0/133                                           | NA                | NA                             | 45        |
| Chickens  | Experimental| 0/17                                            | Oculo-oral onasal | $1 \times 10^5 \text{TCID}_{50}$ | 46        |
|           |             | 0/5                                             | Intranasal        | $1 \times 10^{5.5} \text{PFU}$ | 43        |
|           |             | 0/10                                            | Intrachoanal      | $1 \times 10^{5.4} \text{TCID}_{50}$ | 47        |
|           | Surveillance| 0/153                                           | NA                | NA                             | 45        |
| Ducks     | Experimental| 0/5                                             | Intranasal        | $1 \times 10^{5.5} \text{PFU}$ | 43        |
|           |             | 0/10                                            | Intrachoanal      | $1 \times 10^6 \text{TCID}_{50}$ | 47        |
|           | Surveillance| 0/153                                           | NA                | NA                             | 45        |
| Turkeys   | Experimental| 0/10                                            | Intrachoanal      | $1 \times 10^{5.4} \text{TCID}_{50}$ | 47        |
| Japanese quail | Experimental| 0/10 | Intrachoanal | $1 \times 10^{5.4} \text{TCID}_{50}$ | 47        |
| White Chinese geese | Experimental| 0/10 | Intrachoanal | $1 \times 10^6 \text{TCID}_{50}$ | 47        |

---

aMedian tissue culture infectious dose (TCID_{50}) per animal or plaque-forming unit (PFU).

bNA, not available.
| Country       | First report | Farm characteristics                  | Farm staff/owner COVID-19 status | Reference                                                                 | Additional reports                                                                 |
|--------------|--------------|---------------------------------------|----------------------------------|---------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Netherlands  | 26-April     | Two farms                             | Positive                         | https://promedmail.org/promed-post/?id=20200427.7272289                   | 14-Oct: 67 farms affected; approximately 440 000 mother animals and 2.2 million young mink have been culled (https://promedmail.org/promed-post/?id=20201019.7873326) |
| Spain        | 16-July      | Single farm 93 000 mink                | Positive                         | https://promedmail.org/promed-post/?id=7584560                              |                                                                                      |
| Denmark      | 17-June      | Single farm 11 000 mink               | Not reported                     | https://promedmail.org/promed-post/?id=20200617.7479510                    | 13-Oct: 63 farms affected (https://promedmail.org/promed-post/?id=20201014.7861560) 5-Nov: All mink, approximately 17 million animals, will be culled (https://promedmail.org/promed-post/?id=20201122.7963766) |
| USA, Utah    | 17-August    | Two farms Quarantine                  | Positive                         | https://promedmail.org/promed-post/?id=20200818.7692815                    | 2-Oct-20: Death of 7000-8000 mink within 10 days, 9 sites are in quarantine (https://promedmail.org/promed-post/?id=7847704) |
| Italy        | 27-October   | Single farm                           | Not reported                     | https://promedmail.org/promed-post/?id=7897986                              |                                                                                      |
| Sweden       | 29-October   | Single farm                           | Positive                         | https://promedmail.org/promed-post/?id=20201103.7912846                    | 6-Nov-20: Nine additional farms (total of 10/40) infected (https://promedmail.org/promed-post/?id=7924269) |
| USA, Wisconsin | 5-November | Two farms 5000 mink Depopulation     | Not reported                     | https://promedmail.org/promed-post/?id=7923387                              |                                                                                      |
| Greece       | 13-November  | Two farms Culling                     | Positive                         | https://promedmail.org/promed-post/?id=7944705                              |                                                                                      |
| France       | 22-November  | Single farm 1000 mink                | Not reported                     | https://promedmail.org/promed-post/?id=7965554                              |                                                                                      |
| Poland       | 24-November  | Single farm                           | Not confirmed                    | https://promedmail.org/promed-post/?id=7976927                              |                                                                                      |
| Lithuania    | 26-November  | Single farm 169 dead mink Culling of selected cages | Positive                         | https://promedmail.org/promed-post/?id=7976927                              |                                                                                      |
the SARS-CoV-2 spike glycoprotein was detected at 14 and 22 dpi while neutralizing antibodies were detected at 22 dpi in pigs inoculated by parenteral routes (IM or IV). It was suggested that pigs may be a good model for SARS-CoV-2 immunogenicity studies. In contrast, a Canadian study using 16 8-week-old pigs inoculated with SARS-CoV-2 via an oronasal route did find low susceptibility to infection in these pigs due to detection of viral RNA in nasal wash (2/16 pigs at 3 days post-challenge) and pooled oral fluids from another room (1/2 at 3 days post-challenge), as well as the successful isolation of virus from a pig. Furthermore, 2/16 pigs, unrelated to the SARS-CoV-2 RNA positive pigs, developed low neutralizing antibody titres against SARS-CoV-2 between 11 and 15 days post-challenge.

Little research has been done in ruminants so far; however, a recent study using six 4 to 5-month-old cattle intranasally inoculated with SARS-CoV-2, found low level virus replication and antibody development in 2 of the 6 animals. A sentinel control animal did not become infected. While this may seem concerning, to date there is no indication that cattle play any role in the human pandemic nor are there any reports of naturally infected bovines. For a natural human-to-cattle SARS-CoV-2 infection to happen, cattle need to be in close contact with an infected human and this may not occur frequently in today’s cattle-raising facilities. However, further confirmation of this data is needed and the susceptibility of other ruminant livestock species such as sheep and goats needs to be investigated.

### 4.3 SARS-CoV-2 in farmed mink

SARS-CoV-2 in mink behaves differently compared to other animal species. It is commonly associated with severe clinical outbreaks including high morbidity and mortality in infected farms; however, subclinical disease can also occur. So far, outbreaks have been reported in several European countries and in the USA. As a consequence of the various outbreaks seen in mink farms, several culling interventions have been carried out, as outlined in Table 4. Recently, a Chinese research group investigated the biological properties of SARS-CoV-2 in experimentally infected mink. It was determined that SARS-CoV-2 replicates efficiently in the respiratory tract, as expected, and is transmitted among mink via respiratory droplets. As lesions in mink are similar to humans suffering from COVID-19, the mink model was proposed as a useful animal model to evaluate COVID-19 therapeutics or vaccines.50

### 4.4 SARS-CoV-2 in wildlife species

Investigations into wildlife species are perhaps underrepresented at this point in time. In large cats living in zoos, SARS-CoV-2 has been identified on several occasions, including in tigers and lions in New York, NY, USA in April, in a puma in Pretoria, South Africa in July, and in tigers in the Knoxville, TN, USA in October. All large cats that were confirmed as infected displayed mild respiratory signs, which promoted investigation, and had been in contact with COVID-19 positive animal handlers. In addition to large cats, research macaques can be readily infected under experimental conditions and also appear to present with mild clinical signs. No data is available on macaques or wild cats living in their natural habitats or any other wild animals.

The search for possible SARS-CoV-2 animal reservoirs in wildlife species is akin to the search for a needle in a haystack. In sub-clinically infected animals, SARS-CoV-2 viremia and shedding would be very short-lived and may not be detected even if recently infected animals were tested. Other alternative approaches to investigate the SARS-CoV-2 human-wildlife interface likely need to be pursued and may need to rely on mass sequencing on water, air or pooled faecal samples from common areas such as freshwater reservoirs or feeding areas. Interestingly, in August 2020, China announced regular coronavirus tests at wholesale markets (weekly for major markets, monthly for smaller operations), with a focus on knives used at major stands, workers’ clothing, surfaces, freezers, meat, seafood, sewage, restrooms, garbage trucks and offices.

## 5 SUMMARY

SARS-CoV-2 emerged in the human population towards the end of 2019 and has been spreading at an alarming rate and cases in humans continue to increase. This is predicted to continue until commercial vaccines, which recently became available in selected countries, are approved and have been distributed to a larger number of people, ensuring that a certain proportion of the global population is protected. Pet animals such as cats and dogs do not currently appear to pose a risk to humans; however, continuous monitoring of these animals is warranted. SARS-CoV-2 spillover into farm animals has not been reported to date, but if it happens, it likely happens very sporadically and involves a low number of animals. An exception to this is farmed mink, where SARS-CoV-2 spreads quickly and causes clinical disease in infected animals. As a precaution, nearly all affected mink farms implemented immediate mass culling. The rapid identification of a human-animal spillover event and its removal or containment is critical in safeguarding humans and also other animal species. Careful consideration and attention should be given to other future SARS-CoV-2 spillover events into the animal population in order to effectively control the ongoing pandemic.

**ORCID**

Tanja Opriessnig [https://orcid.org/0000-0001-9755-8411](https://orcid.org/0000-0001-9755-8411)

Yao-Wei Huang [https://orcid.org/0000-0001-9642-0904](https://orcid.org/0000-0001-9642-0904)
REFERENCES

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

2. Patel U, Malik P, Mehta D, et al. Early epidemiological indicators, outcomes, and interations of COVID-19 pandemic: a systematic review. J Glob Health. 2020;10(2):20506.

3. Boni MF, Lemey P, Jiang X, et al. Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic. Nat Microbiol. 2020.5(11):1408-1417.

4. Wong ACP, Li X, Lau SKP, Woo PCY. Global epidemiology of bat coronaviruses. Viruses. 2019;11:2.

5. Murakami S, Kitamura T, Suzuki J, et al. Detection and characterization of bat sarbecovirus phylogenetically related to SARS-CoV-2. Japan. Emerg Infect Dis. 2020;26(12):3025-3029.

6. Burki T. The origin of SARS-CoV-2. Lancet Infect Dis. 2020;20(9):1018-1019.

7. Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Travel Med. 2020;27(2):taa021.

8. Opriessnig T, Huang Y-W. Further information on possible animal sources for human COVID-19. Xenotransplantation. 2020;27(6):e12651.

9. Martinez-Hernández F, Isaak-Delgado AB, Alfonso-Toledo JA, et al. Assessing the SARS-CoV-2 threat to wildlife: Potential risk to a broad range of mammals. Percept Ecol Conserv. 2020;18(4):223-234.

10. Damas J, Hughes GM, Keough KC, et al. Broad host range of SARS-CoV-2 predicted by comparative and structural analysis of ACE2 in vertebrates. Proc Natl Acad Sci USA. 2020;117(36):22311-22322.

11. Pickering BS, Smith G, Pinette MM, et al. Susceptibility of domestic swine to experimental infection with severe acute respiratory syndrome coronavirus 2. Emerg Infect Dis. 2021;27(1):104-112.

12. Ulrich L, Wernike K, Hoffmann D, Mettenleiter TC, Beer M. Experimental infection of cattle with SARS-CoV-2. Emerg Infect Dis. 2020;26(12):2979-2981.

13. Santini JM, Edwards S JL. Host range of SARS-CoV-2 and implications for public health. Lancet Microbe. 2020;1(4):e141-e142.

14. Luan J, Lu Y, Jin X, Zhang L. Spike protein recognition of mammalian ACE2 predicts the host range and an optimized ACE2 for SARS-CoV-2 infection. Biochem Biophys Res Commun. 2020;526(1):165-169.

15. Xu L, Yu DD, Ma YH, et al. COVID-19-like symptoms observed in Chinese tree shrews infected with SARS-CoV-2. Zool Res. 2020;41(5):517-526.

16. Cao J, Yang EB, Su JJ, Li Y, Chow P. The tree shrews: adjuncts and alternatives to primates for models for biomedical research. J Med Primatol. 2003;32(3):123-130.

17. Parrish CR, Holmes EC, Morens DM, et al. Cross-species virus transmission and the emergence of new epidemic diseases. Microbiol Mol Biol Rev. 2008;72(3):457-470.

18. Sit THC, Brackman CJ, Ip SM, et al. Infection of dogs with SARS-CoV-2. Nature. 2020;586(7831):776-778.

19. Garigliani M, Van Laere A-S, Clerc C, et al. SARS-CoV-2 natural transmission from human to cat, Belgium, March 2020. Emerg Infect Dis. 2020;26(12):3069-3071. http://dx.doi.org/10.3201/eid2612.200223

20. Cioczar A, Jakab F, Valencak TG, et al. Companion animals likely do not spread COVID-19 but may get infected themselves. GeroScience. 2020;42(5):1229-1236.

21. Halfmann PJ, Hatta M, Chiba S, et al. Transmission of SARS-CoV-2 in Domestic Cats. N Engl J Med. 2020;383(6):592-594.

22. Bosco-Lauth AM, Hartwig AE, Porter SM, et al. Experimental infection of domestic dogs and cats with SARS-CoV-2: pathogenesis, transmission, and response to reexposure in cats. Proc Natl Acad Sci USA. 2020;117(42):26382-26388.

23. Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, et al. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans. Science. 2020;eabe5901. https://doi.org/10.1126/science.abe5901. [Epub ahead of print].

24. Enserkink M. Coronavirus rips through Dutch mink farms, triggering culls. Science. 2020;368(6496):1169.

25. Muted Covid-19 found in mink farms in Denmark. Vet Rec. 2020;187(10):381.

26. Longdon B, Brockhurst MA, Russell CA, Welsh JJ, Jiggins FM. The evolution and genetics of virus host shifts. PLoS Pathog. 2014;10(11):e1004395.

27. Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, et al. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans. Science. 2020;eabe5901. https://doi.org/10.1126/science.abe5901.

28. Singh PK, Kulsum U, Rufai SB, Mudliar SR, Singh S. Mutations in SARS-CoV-2 leading to antigenic variations in spike protein: a challenge in vaccine development. J Lab Physicians. 2020;12(2):154-160.

29. Mallappa S. COVID mink analysis shows mutations are not dangerous - yet. Nature. 2020;587(7834):340-341. https://doi.org/10.1038/d41586-020-03218-z

30. Zhao Z, Li H, Wu X, et al. Moderate mutation rate in the SARS-coronavirus genome and its implications. BMC Evol Biol. 2020;4(1):21.

31. Nakagawa S, Miyazawa T. Genome evolution of SARS-CoV-2 and its virological characteristics. Inflamm Regen. 2020;40:17.

32. Callaway E. The coronavirus is mutating - does it matter? Nature. 2020;585(7824):174-177.

33. Sailleau C, Dumarest M, Vanhomwegen J, et al. First detection and genome sequencing of SARS-CoV-2 in an infected cat in France. Transbound Emerg Dis. 2020;67(6):2324-2328. https://doi.org/10.1111/tbed.13659.

34. Musso N, Costantino A, La Spina S, et al. New SARS-CoV-2 infection detected in an Italian pet cat by RT-qPCR from deep pharyngeal swab. Pathogens. 2020;9(7):746.

35. Segalés J, Puig M, Rodon J, et al. Detection of SARS-CoV-2 in a cat owned by a COVID-19-affected patient in Spain. Proc Natl Acad Sci USA. 2020;117(40):24790-24793.

36. Stevanovic V, Vilbic-Cavlek T, Tabain I, et al. Seroprevalence of SARS-CoV-2 infection among pet animals in Croatia and potential public health impact. Transbound Emerg Dis. 2020. https://doi.org/10.1111/tbed.13924. Online ahead of print.

37. Zhang Q, Zhang H, Gao J, et al. A serological survey of SARS-CoV-2 in cat in Wuhan. Emerg Microbes Infect. 2020;9(1):2013-2019.

38. Gaudreault NN, Trujillo JD, Carossino M, et al. SARS-CoV-2 infection, disease and transmission in domestic cats. Emerg Microbes Infect. 2020;9(1):2322-2332.

39. Sia SF, Yan LM, Chin AWH, et al. Pathogenesis and transmission of SARS-CoV-2 in golden hamsters. Nature. 2020;583(7818):834-838.

40. Chan JF, Zhang AJ, Yuan S, et al. Simulation of the clinical and pathological manifestations of coronavirus disease 2019 (COVID-19) in a Golden Syrian hamster model: Implications for disease pathogenesis and transmissibility. Clin Infect Dis. 2020;71(9):2428-2446.

41. Kim YI, Kim SG, Kim SM, et al. Infection and rapid transmission of SARS-CoV-2 in ferrets. Cell Host Microbe. 2020;27(5):704-709. e702.

42. Richard M, Kok A, de Meulder D, et al. SARS-CoV-2 is transmitted via contact and via the air between ferrets. Nature Commun. 2020;11(1):3496.

43. Shi J, Wen Z, Zhong G, et al. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. Science. 2020;368(6494):1016-1020.

44. Patterson EI, Elia G, Grassi A, et al. Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy. Nat Commun. 2020;11(1):6231.
45. Deng J, Jin Y, Liu Y, et al. Serological survey of SARS-CoV-2 for experimental, domestic, companion and wild animals excludes intermediate hosts of 35 different species of animals. Transbound Emerg Dis. 2020;67(4):1745-1749.

46. Schlottau K, Rissmann M, Graaf A, et al. SARS-CoV-2 in fruit bats, ferrets, pigs, and chickens: an experimental transmission study. Lancet Microbe. 2020;1(5):e218-e225.

47. Suarez DL, Pantin-Jackwood MJ, Swayne DE, Lee SA, DeBlois SM, Spackman E. Lack of susceptibility to SARS-CoV-2 and MERS-CoV in poultry. Emerg Infect Dis. 2020;26(12):3074-3076.

48. Meekins DA, Morozov I, Trujillo JD, et al. Susceptibility of swine cells and domestic pigs to SARS-CoV-2. Emerg Microbes Infect. 2020;9(1):2278-2288.

49. Vergara-Alert J, Rodon J, Carrillo J, et al. Pigs are not susceptible to SARS-CoV-2 infection but are a model for viral immunogenicity studies. Transbound Emerg Dis. 2020. https://doi.org/10.1111/tbed.13861. Online ahead of print.

50. Shuai L, Zhong G, Yuan Q, et al. Replication, pathogenicity, and transmission of SARS-CoV-2 in minks. Nat Sci Rev. 2020;nwaa291: https://doi.org/10.1093/nsr/nwaa291. (accepted manuscript online ahead of print)

51. McAloose D, Laverack M, Wang L, et al. From people to Panthera: natural SARS-CoV-2 infection in tigers and lions at the Bronx Zoo. MBio. 2020;11(5):e02220-20.

52. Cleary SJ, Pitchford SC, Amison RT, et al. Animal models of mechanisms of SARS-CoV-2 infection and COVID-19 pathology. Br J Pharmacol. 2020;177(21):4851-4865.

53. Deng W, Bao L, Gao H, et al. Ocular conjunctival inoculation of SARS-CoV-2 can cause mild COVID-19 in rhesus macaques. Nat Commun. 2020;11(1):4400.

54. Nantachit N, Khamrin P, Kumthip K, Malasao R, Maneekarn N. Molecular surveillance and genetic analyses of bufavirus in environmental water in Thailand. Infect Genet Evol. 2019;75:104013.

55. Bailey ES, Choi JY, Zemke J, Yondon M, Gray GC. Molecular surveillance of respiratory viruses with bioaerosol sampling in an airport. Trop Dis Travel Med. 2018;4:11.

56. Anderson BD, Lednicky JA, Torremorell M, Gray GC. The use of bioaerosol sampling for airborne virus surveillance in swine production facilities: a mini review. Front Vet Sci. 2017;4:121.

How to cite this article: Opriessnig T, Huang Y-W. Third update on possible animal sources for human COVID-19. Xenotransplantation. 2021;28:e12671. https://doi.org/10.1111/xen.12671