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Update on possible animal sources for COVID-19 in humans

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.
Emails: Tanja.Opriessnig@roslin.ed.a.ac.uk, tanjaopr@iatate.edu

Since our commentary on the likelihood of pigs transmitting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to humans published in March 2020,1 the World Health Organization (WHO) has upgraded SARS-CoV-2 infection to a global pandemic (https://www.who.int/dg/speeches/detail/who-director-general-s-open-remark-at-the-media-briefing-on-covid-19---11-march-2020) and the virus has spread to all continents with direct impact in most countries. Updated SARS-CoV-2 data in humans are provided in Table 1. This synopsis summarizes the latest findings on animal sources that could pose a risk for human SARS-CoV-2 infection and hence may be important during xenotransplantation.

The novel SARS-CoV-2 was initially observed with severe lung disease designated as coronavirus disease 2019 (COVID-19) in a cluster of patients in Wuhan, Hubei Province in China during December 2019.2 Coronavirus species typically cause respiratory and gastrointestinal sickness in both humans and animals.3 It is recognized that SARS-CoV-2 can be transmitted through aerosols and direct or indirect contact.4-6 However, the role of animals in human infections is less clear. One of the earliest published studies investigating the ability of SARS-CoV-2 to replicate in various animal species found that the virus does not infect farm animals including pigs, chickens, and ducks.7 In support of these early results, an ongoing study conducted at the Friedrich Loeffler Institute in Germany further confirmed that pigs and chickens are not susceptible to intranasal infection with SARS-CoV-2 (https://promedmail.org/promed-post/?id=7196506). Results from experimental infection trials are summarized in Table 2. Furthermore, a large Chinese study investigated naturally occurring SARS-CoV-2 infection in various animal species by examining antibody levels and included serum samples from 187 pigs, 107 cattle, 133 sheep, 18 horses, 153 chickens, and 154 ducks which all tested negative.

It appears that ferrets, cats and to some degree also dogs are permissive to SARS-CoV-2 infection. In ferrets, experimental infection resulted in virus replication in the upper respiratory tract for up to 8 days without clinical signs or mortality.7 These findings were essentially confirmed by other groups who also established that naïve ferrets can be infected via contact exposure (https://promedmail.org/promed-post/?id=7196506) or airborne transmission.9,10 Furthermore, minks with naturally acquired SARS-CoV-2 infection have been identified (Table 3) confirming that the Mustelidae family, which includes ferrets, minks but also weasels, badgers, and otters, appears susceptible to SARS-CoV-2 infection.

Evidence that pets may be susceptible to SARS-CoV-2 arose first via an experimental infection trial.7 Specifically, 2-6 months old cats were intranasally inoculated with SARS-CoV-2 and viral RNA was detected in the respiratory tract 6 days post-infection. When the cats were placed in contact with uninfected cats, SARS-CoV-2 transmission occurred after 3 days and antibodies against SARS-CoV-2 were detected in infected and exposed cats (Table 2).7 Similar findings were reproduced in US cats recently.11 Additional accumulated evidence during a seroprevalence study further supports that SARS-CoV-2 is indeed capable of entering the feline population.12 A total of 145 cat serum samples collected from pet hospitals and animal shelters in Wuhan before and during the COVID-19 outbreak were tested. Approximately 13.7% (15/102) of the samples collected during the outbreak were found positive by three assays while 39 samples collected prior to the COVID-19 outbreak were all negative.12 Furthermore, several domestic cats, lions, and tigers with naturally acquired SARS-CoV-2 infection have been identified (Table 3).
The susceptibility of dogs to SARS-CoV-2 has also been investigated. After experimental infection they may become infected at a low level with limited transmission. Natural infection, as evidenced by the presence of antibodies, SARS-CoV-2 RNA or both, has been identified in selected dogs in close contact with COVID-19 patients (Table 3). A recent French study, which investigated nine cats and 12 dogs in close contact with a cluster of COVID-19 patients, was unable to detect evidence of SARS-CoV-2 infection in any of the animals. Finally, the Chinese serosurveillance study that investigated farm animals also tested serum samples from 487 dogs and 87 cats collected between November 2019 and March 2020. All samples were negative for SARS-CoV-2 antibodies, in accordance with the French study.

In summary, since SARS-CoV-2 emerged in the human population towards the end of 2019, it has been spreading at a high rate. There is strong evidence that SARS-CoV-2 from COVID-19 infected humans can spill over to animal species within the families Mustelidae, Felinae, and Caninae. Infections are frequently subclinical but occasional clinical signs can be observed (Table 3). Based on available serological surveys, these are likely localized rare events; the true extent of human-to-animal infections requires further investigations. Moreover, animal-to-human SARS-CoV-2 infection as well as natural animal-to-animal transmission has yet to be confirmed and none of the species considered to be susceptible to the virus at this point are presently used for xenotransplantation. Despite not being affected by SARS-CoV-2 directly, pigs are being used to test novel SARS-CoV-2 vaccines for possible human use (https://www.pirbright.ac.uk/news/2020/03/pirbright-begins-testing-new-coronavirus-vaccines-animals-help-combat-covid-19).
### Table 3: Documented naturally acquired SARS-CoV-2 infections in different animal species

| Family       | Species | Date    | Location   | Clinical signs                                      | SARS-CoV-2 test results | Comments                                | Reference                                                                 |
|--------------|---------|---------|------------|----------------------------------------------------|-------------------------|-----------------------------------------|--------------------------------------------------------------------------|
| **Felidae**  | Domestic cat | 18-Mar | Belgium   | Respiratory signs, vomiting, diarrhea              | Positive (feces and vomit) | ND ND | COVID-19 household Cat recovered after 9 d | [https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/COVID-19/Belgium_28.03.20.pdf](https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/COVID-19/Belgium_28.03.20.pdf) |
|              |         | 02-Apr  | Hong Kong | None                                               | Positive (oral, nasal and rectal swabs) | ND ND | COVID-19 household                          | [https://promedmail.org/promed-post/?id=7175340](https://promedmail.org/promed-post/?id=7175340) |
|              |         | 22-Apr  | New York, USA | Sneezing, Ocular discharge                        | Positive                | Positive ND ND | COVID-19 household Outdoor access          | [https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=34086](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=34086) |
|              |         | 01-May  | France     | Mild respiratory and digestive signs               | Positive (rectal swab)  | ND ND | COVID-19 household 1/2 cats in the household affected | [https://promedmail.org/promed-post/?id=20200501.7289409](https://promedmail.org/promed-post/?id=20200501.7289409) |
|              |         | 08-May  | Spain      | Respiratory signs                                  | Positive (nasal cavity, enteric lymph node) | ND ND | COVID-19 household                          | [https://english.elpais.com/society/2020-05-08/spain-records-its-first-case-of-a-cat-with-coronavirus.html](https://english.elpais.com/society/2020-05-08/spain-records-its-first-case-of-a-cat-with-coronavirus.html) |
| Tiger        |         | 27-Mar  | Bronx Zoo, New York, USA | Dry cough, Wheezing | Positive | ND ND | Infection assumed by asymptotic zoo employee; clinical signs in five tigers and three lions; testing was done for one tiger and one lion | [https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=33885](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=33885) |
| Lion         |         |         |           |                                                    | Positive                | ND ND |                                         |                                                                          |
| **Canidae**  | Dog     | 26-Feb  | Hong Kong | None                                               | Positive (nasal swabs on 26-Feb, 28-Feb, 2-Mar, 5-Mar, and 9-Mar) | Positive Negative | COVID-19 household Pomeranian dog, 17 y old | [https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=33762](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=33762) |
|              |         | 17-Mar  | Hong Kong | None                                               | Positive (nasal and oral swabs on 18-Mar, 19-Mar; rectal swab on 18-Mar) | Positive Positive | COVID-19 household German Shepherd, 2.5 y old; 1/2 dogs infected | [https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=33892](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport?Review?reportid=33892) |
|              |         | 29-Apr  | North Carolina, USA | Mild cough | Positive | ND ND | COVID-19 household Pug                      | [https://edition.cnn.com/2020/04/28/us/coronavirus-us-pug-wellness-trnd/index.html](https://edition.cnn.com/2020/04/28/us/coronavirus-us-pug-wellness-trnd/index.html) |
| **Mustelidae** | Mink   | 23-Apr  | The Netherlands | Gastrointestinal and respiratory signs, Increased mortality | Positive ND | ND | Mink farm 1 Two employees with COVID-19 signs | [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](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) |
|              |         | 25-Apr  |           | Pneumonia problems, Increased mortality            | Positive ND | ND | Mink farm 2 One employee with COVID-19 signs |                                                                          |

ND = Not done.
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ORCID
Tanja Opriessnig https://orcid.org/0000-0001-9642-0904

REFERENCES
1. Opriessnig T, Huang YW. Coronavirus disease 2019 (COVID-19) outbreak: could pigs be vectors for human infections? Xenotransplantation. 2020;27:e12591.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
3. Pal M, Berhanu G, Desalegn C, Kandi V. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): an update. Cureus. 2020;12:e7423.
4. Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. Int J Oral Sci. 2020;12:9.
5. Anonymous. Early epidemiological and clinical characteristics of 28 cases of coronavirus disease in South Korea. Osong Public Health Res Perspect. 2020;11:8-14.
6. Godri Pollitt KJ, Peccia J, Ko Al, et al. COVID-19 vulnerability: the potential impact of genetic susceptibility and airborne transmission. Hum Genomics. 2020;14:17.
7. 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.
8. 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. https://doi.org/10.1111/tbed.13577. [Epub ahead of print].
9. Kim YL, Kim SG, Kim SM, et al. Infection and rapid transmission of SARS-CoV-2 in ferrets. Cell Host Microbe. 2020;27(5):704-709.e2.
10. Richard M, Kok A, de Meulder D, et al. SARS-CoV-2 is transmitted via contact and via the air between ferrets. bioRxiv. 2020. https://doi.org/10.1101/2020.04.16.044503
11. Halfmann PJ, Hatta M, Chiba S, et al. Transmission of SARS-CoV-2 in domestic cats. N Engl J Med. 2020. https://doi.org/10.1056/NEJMc2013400. [Epub ahead of print].
12. Zhang Q, Zhang H, Huang K, et al. SARS-CoV-2 neutralizing serum antibodies in cats: a serological investigation. bioRxiv. 2020. https://doi.org/10.1101/2020.04.01.021196
13. Temmam S, Barbarino A, Maso D, et al. Absence of SARS-CoV-2 infection in cats and dogs in close contact with a cluster of COVID-19 patients in a veterinary campus. bioRxiv. 2020. https://doi.org/10.1101/2020.04.07.029090
14. Sit THC, Brackman CJ, Ip SM, et al. Infection of dogs with SARS-CoV-2. Nature. 2020. https://doi.org/10.1038/s41586-020-2334-5