

Natural infections of SARS-CoV-2 increased in animals: How should humans interact with animals?

To the editor,

The Middle East respiratory syndrome coronavirus (MERS-CoV), along with the severe acute respiratory syndrome coronavirus (SARS-CoV), and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), are three emerging coronaviruses with significant public health implications in the 21st century. SARS-CoV-2, in particular, has caused an unprecedented global pandemic, spreading to over 200 countries. As of the manuscript submission date, more than 450 million people were infected with SARS-CoV-2, with nearly 6 million of those infected dying (The data from World Health Organization).

The origin (bat, snake, and pangolin) of SARS-CoV-2 has been debated since its first discovery in humans.¹⁻⁴ Although probable bat-origin SARS-CoV and human-origin SARS-CoV-2 had 96% nucleotide similarity, they were not the same virus. More and more human-to-animal transmissions of SARS-CoV-2 have been reported in several countries over time.⁵

This study performed a meta-analysis about natural infections of SARS-CoV-2 in animals. In detail, PubMed, a widely concerned database, was used. The systematic search was performed using a group of (medical subject headings, MeSH) terms and text words, such as (Covid OR SARS-CoV-2) AND (animal OR pet OR animal infection OR cat OR dog OR ferret OR tiger OR lion OR deer OR other animals). From January 1, 2020, to December 31, 2021, 9967 papers were searched. Finally, 105 papers about SARS-CoV-2 natural infection in animals were collected and used for analysis. With every half year as a calculation cycle, the number of published papers in PubMed gradually increased (Figure 1A). Serological, molecular, and double evidence were linked to 32, 26, and 47 papers, respectively. The cat (39/105 papers) was the most common natural infection host among infected animals. Cats and dogs were still the main natural infection hosts in 26 multispecies studies (Figure 1B). These findings suggested that cats and dogs may be particularly vulnerable to SARS-CoV-2 infection.^{5,6} Most papers came from American and European countries (Figure 2), consistent with the current coronavirus disease 2019 (COVID-19) epidemic.

Almost all animal infections in these natural SARS-CoV-2 infection studies were caused by infected humans. It is worth noting that transmission from animal to animal or animal to human occasionally occurred.⁷ In reality, humans and animals share the same environment and could potentially infect each other. As a result, a critical question about human-animal

interactions must be addressed. Our recommendation was as follows:

Companion animals (particularly cats and dogs) had the most human contact and the highest prevalence of SARS-CoV-2. First, pet owners should practice good biosecurity and family self-protection, including limiting going out, limiting close contact with pets, wearing masks, receiving necessary vaccinations, and conducting regular surveillance, all of which can help reduce potential human-to-animal transmission.⁸ Second, to avoid potential animal-to-animal transmission, pets should avoid going out and having close contact with stray animals. Furthermore, pet owners should regularly disinfect their shared living environment to avoid viral transmission in the contaminated environment.

Zoo animals (such as tigers and lions) were typically raised in enclosed areas in zoos. To reduce or prevent their infection, we need to do two things. Animal keepers or veterinarians should first strengthen viral surveillance to avoid potential human-to-animal transmission. In addition, stray animals, particularly those with climbing abilities (cats, squirrels, and rodents), should be ejected from zoos to prevent possible animal-to-animal transmission.

Most farm animals, such as pigs, chickens, and cattle, were resistant to SARS-CoV-2, but fur animals (such as minks and ferrets) were highly susceptible.⁸⁻¹⁰ Due to the infection of keepers, many mink farms in Denmark tested positive for SARS-CoV-2, and there was even human-to-human transmission. To reduce human-to-animal and/or animal-to-animal transmission, keepers, veterinarians, and stray animals should be well-managed on farms.

Wild animals (like deer) and stray animals (like dogs and rodents) can roam freely. However, in the United States, wild white-tailed deer had a high seroconversion rate, implying that the wild deer had been exposed to SARS-CoV-2.¹¹ Field investigators (such as researchers, hunters, and tourists) and wild animals should be better monitored to prevent SARS-CoV-2 from spreading. In addition, necessary viral contamination indicators (such as mussels) must be established in the wild environment.¹²

A laboratory animal is a type of animal used in scientific research. Many lab animals, such as transgenic rodents, and ferrets, were susceptible to SARS-CoV-2, making them good animal models. Although there have been few reports of SARS-CoV-2 spreading from lab animals to humans, researchers should follow the biosecurity protocol and take appropriate biosafety precautions, such as wearing protective clothing and masks.

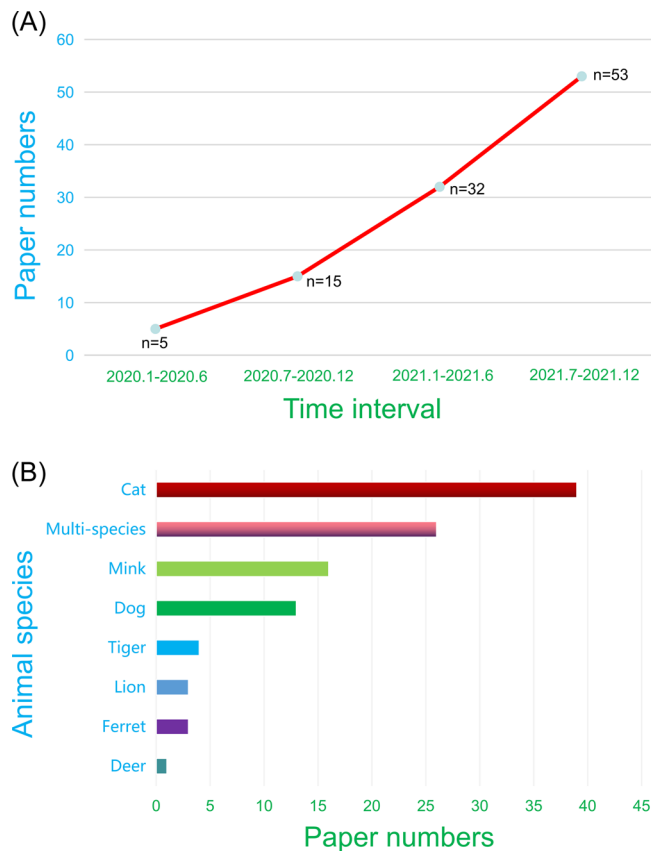


FIGURE 1 SARS-CoV-2 infection in animals by paper numbers, sorted by published time and animal species. (A) Paper numbers of SARS-CoV-2 infection in animals by publication date; (B) Paper numbers of SARS-CoV-2 infection in animals by animal species. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

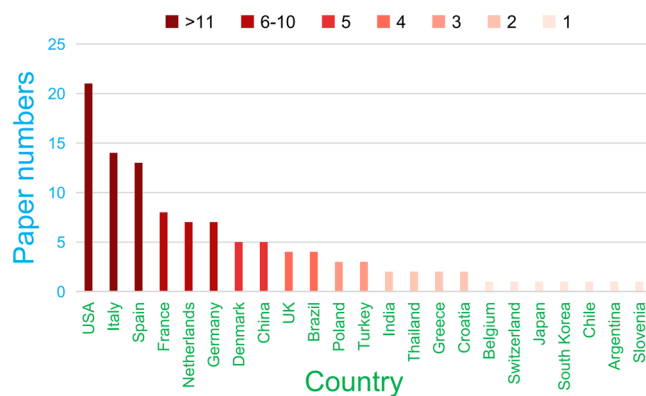


FIGURE 2 SARS-CoV-2 infection in animals by paper numbers, by country of collection. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

In conclusion, SARS-CoV-2 is found widely in humans, animals, and the environment. Humans are the most important factor in SARS-CoV-2 control. We can discover a transmission route, control the infection, and develop vaccines and antiviral drugs. However, in addition to ongoing trade and migration in different countries and

regions, the viral mutation increases, contributing to the spread of SARS-CoV-2. Perhaps, we will continue to fight SARS-CoV-2 in the coming years.

AUTHOR CONTRIBUTIONS

Shao-Lun Zhai, Chun-Ling Li, and Ming-Fei Sun are the cofirst authors of this paper. They collected the data, analyzed it, and drafted the paper for the work. Jian-Feng Zhang, Chunfu Zheng, and Ming Liao are co-corresponding authors of this paper, they did the financial support, review, and final approval of the paper to be published. All authors read and approved the final manuscript.

ACKNOWLEDGMENTS





This study was supported by the following grants: the grant (No. 2020B0202080004) from the Guangdong Provincial Department of Science and Technology, the grant (No. 202103000096) from Guangzhou Science and Technology Bureau, the grant (No. 2021ZZ003) from Maoming Branch, Guangdong Laboratory for Lingnan Modern Agricultural, and special fund (Nos. R2020PY-JC001 and XTXM202202) from Guangdong Academy of Agricultural Sciences.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in PubMed at <https://pubmed.ncbi.nlm.nih.gov/>.

Shao-Lun Zhai¹ 
 Chun-Ling Li¹
 Ming-Fei Sun¹ 
 Jian-Feng Zhang¹
 Chunfu Zheng² 
 Ming Liao¹ 

¹Institute of Animal Health, Guangdong Academy of Agricultural Sciences, Key Laboratory of Livestock Disease Prevention of Guangdong Province, Scientific Observation and Experiment Station of Veterinary Drugs and Diagnostic Techniques of Guangdong Province, Ministry of Agriculture and Rural Affairs, Maoming Branch, Guangdong Laboratory for Lingnan Modern Agriculture, Guangzhou, China
 Email: zhaishaolun@163.com

²Department of Immunology, School of Basic Medical Sciences, Fujian Medical University, Fuzhou, China
 Email: lclclaire@163.com

Correspondence

Jian-Feng Zhang and Ming Liao, Institute of Animal Health, Guangdong Academy of Agricultural Sciences, Key Laboratory of Livestock Disease Prevention of Guangdong Province, Scientific Observation and Experiment Station of Veterinary Drugs and Diagnostic Techniques of Guangdong Province, Ministry of

Agriculture and Rural Affairs, Guangzhou 510640, China.
 Email: zhang-jianfeng@139.com and mliao@scau.edu.cn
 Chunfu Zheng, Department of Immunology, School of Basic Medical
 Sciences, Fujian Medical University, Fuzhou 350004, China.
 Email: zheng.alan@hotmail.com

Shao-Lun Zhai, Chun-Ling Li and Ming-Fei Sun are co-first authors.

ORCID

Shao-Lun Zhai  <https://orcid.org/0000-0003-3217-2256>

Ming-Fei Sun  <https://orcid.org/0000-0001-5313-8239>

Chunfu Zheng  <http://orcid.org/0000-0002-8797-1322>

Ming Liao  <https://orcid.org/0000-0001-8731-4528>

REFERENCES

- Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020; 579(7798):270-273.
- Liu Z, Xiao X, Wei X, et al. Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2. *J Med Virol*. 2020;92(6):595-601.
- Xiao K, Zhai J, Feng Y, et al. Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. *Nature*. 2020;583(7815):286-289.
- Guo H, Hu B, Si HR, et al. Identification of a novel lineage bat SARS-related coronaviruses that use bat ACE2 receptor. *Emerg Microbes Infect*. 2021;10(1):1507-1514.
- Meekins DA, Gaudreault NN, Richt JA. Natural and experimental SARS-CoV-2 infection in domestic and wild animals. *Viruses*. 2021; 13(10):1993.
- Li X. Cats under the shadow of the SARS-CoV-2 pandemic. *Transbound Emerg Dis*. 2020;67(4):1416-1417.
- 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*. 2021;371(6525):172-177.
- Liu Y, Hu G, Wang Y, et al. Functional and genetic analysis of viral receptor ACE2 orthologs reveals a broad potential host range of SARS-CoV-2. *Proc Natl Acad Sci U S A*. 2021;118(12): e2025373118.
- 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.
- Sreenivasan CC, Thomas M, Wang D, Li F. Susceptibility of livestock and companion animals to COVID-19. *J Med Virol*. 2021;93(3): 1351-1360.
- Chandler JC, Bevins SN, Ellis JW, et al. SARS-CoV-2 exposure in wild white-tailed deer (*Odocoileus virginianus*). *Proc Natl Acad Sci U S A*. 2021;118(47):e2114828118.
- Le Guernic A, Palos Ladeiro M, Boudaud N, et al. First evidence of SARS-CoV-2 genome detection in zebra mussel (*Dreissena polymorpha*). *J Environ Manage*. 2022;301:113866.