

# Coronavirus disease 2019 (COVID-19) outbreak: Could pigs be vectors for human infections?

Tanja Opriessnig<sup>1,2</sup> | Yao-Wei Huang<sup>3</sup>

<sup>1</sup>The Roslin Institute and The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Midlothian, UK

<sup>2</sup>Department of Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames, IA, USA

<sup>3</sup>Institute 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.ac.uk; tanjaopr@iatate.edu

## Funding information

University of Edinburgh, Roslin Institute, Grant/Award Number: BBS/E/D/20002173 and BBS/E/D/20002174; Zhejiang University, Grant/Award Number: 2020XGZX084

Coronaviruses (CoVs) have recently received an extraordinary level of global attention due to the discovery of a novel high pathogenic human coronavirus (CoV) in China in December 2019.<sup>1</sup> CoVs are positive-sense RNA viruses that belong to the subfamily *Orthocoronavirinae* in the family *Coronaviridae* (Source: International Committee on Taxonomy of Viruses—ICTV, Taxonomy history: *Orthocoronavirinae*. Accessed January 24, 2020). This family can be divided into four genera,  $\alpha$ -CoVs,  $\beta$ -CoVs,  $\gamma$ -CoVs, and  $\delta$ -CoVs.<sup>2</sup> CoV in humans are common (Table 1), often associated with mild cold symptoms, and include the  $\alpha$ -CoVs HCoV-229E<sup>3</sup> and HCoV-NL63,<sup>4</sup> and the  $\beta$ -CoVs HCoV-OC43<sup>5</sup> and HCoV-HKU1.<sup>6</sup> In addition, to date three high pathogenic CoVs (all  $\beta$ -CoVs) are recognized in humans and characterized by moderate (MERS-CoV) or high (SARS-CoV, SARS-CoV-2) transmission rates and association with mortality (Table 2).

During 2002–2003 in Guangdong province in China, Severe Acute Respiratory Syndrome (SARS) CoV (SARS-CoV) was discovered.<sup>7–9</sup> From South-East Asia, the first larger SARS-CoV outbreak spread to Europe and North America in 2003<sup>10</sup> and was followed by a smaller outbreak in a laboratory in China during 2004.<sup>11</sup> Since 2004, no known cases of SARS-CoV have been reported. During 2012, the Middle East Respiratory Syndrome (MERS) CoV was recognized in the Middle East region.<sup>12</sup> Finally, in December 2019 a novel CoV (2019-nCoV), later named SARS-CoV-2, was associated with severe lung disease in a cluster of patients in Wuhan, Hubei Province in China, and consequently reported to the World Health Organization.<sup>1</sup> Since the lung disease has been designated as CoV disease 2019 (COVID-19).<sup>13</sup> Interestingly, all currently recognized high pathogenic CoVs in humans appear to have spilled over from bats or other wildlife sources.<sup>14</sup>

Therefore, concerns for further interspecies transmissions of SARS-CoV-2 from humans to other species may be justified.

Pigs play a major role in xenotransplantation due to their organ similarity with humans. Pigs are susceptible to several CoVs including the  $\alpha$ -CoVs transmissible gastroenteritis virus (TGEV),<sup>15</sup> porcine epidemic diarrhea virus (PEDV),<sup>16</sup> porcine respiratory coronavirus (PRCV),<sup>17</sup> and the recently emerging swine acute diarrhea syndrome coronavirus (SADS-CoV)<sup>18,19</sup> which like SARS-CoV or MERS-CoV appears to have originated from bats. Besides these  $\alpha$ -CoVs, pigs are also susceptible to a  $\beta$ -CoV, porcine hemagglutinating encephalomyelitis virus (PHEV),<sup>20</sup> and a  $\delta$ -CoV, porcine deltacoronavirus (PDCoV)<sup>21</sup> (Table 1). As outlined, pigs have their own range of CoVs and humans have their own range of CoVs with no apparent overlap. It is however interesting to note that CoVs in humans mainly target the respiratory tract whereas CoVs in pigs mainly target the enteric system (Table 1). In pigs, there is only a single CoV associated with respiratory infections, PRCV, commonly resulting in mild disease and lesions<sup>22,23</sup> and hence not considered of importance to pork producers. Prevention in the form of vaccines is not in place for PRCV.

Only few studies have investigated if pigs can become infected with SARS-CoV or MERS-CoV and hence have determined if pigs could be a source of infection for humans. During a survey involving six domestic animal species including pigs and 242 individual animals in China, SARS-CoV RNA was detected in a single pig.<sup>24</sup> Furthermore, two pigs among the 242 animals surveyed were SARS-CoV antibody positive. The authors concluded that SARS-CoV interspecies transmission events occur and possibly pose a risk to humans.<sup>24</sup> In another study, 6-week-old pigs and chickens were experimentally infected with SARS-CoV using intravenous, intranasal, ocular, and oral routes.<sup>25</sup>

**TABLE 1** Comparison of CoVs present in humans and pigs based on the genus level including year of discovery and target site

Human CoVs			Pig CoVs		
Virus	First reported or recognized, location	Target site and severity <sup>a</sup>	Virus	First reported or recognized, location	Target site and severity <sup>a</sup>
$\alpha$ -CoVs	HCoV-229E	1966, USA	TGEV	1946, USA	Enteric (S)
	HCoV-NL63	2004, the Netherlands	PEDV	1971, UK	Enteric (S)
			PRCV	1986, Belgium	Respiratory (M)
			SADS-CoV	2017, China	Enteric (M)
$\beta$ -CoVs	HCoV-OC43	1967, USA	PHEV	1962, Canada	Respiratory, peripheral and central nervous system (M)
	SARS-CoV	2002, China			
	HCoV-HKU1	2005, China			
	MERS-CoV	2012, Middle East			
	SARS-CoV-2	2019, China			
$\delta$ -CoVs			PDCoV	2012, China	Enteric (M)

<sup>a</sup>M = mild and for respiratory disease limited to the upper respiratory system. S = severe; especially in naïve populations.

**TABLE 2** Facts on high pathogenic human CoVs

Virus	Time of circulation	Laboratory confirmed cases	Deaths	Case fatality rate	Country distribution
SARS-CoV <sup>a</sup>	2002-2003	8096	774	9.6%	26
MERS-CoV <sup>b</sup>	2012-ongoing	2494	853	35%	27
SARS-CoV-2 <sup>c</sup>	2019-ongoing	153 517	5735	3.7%	144

<sup>a</sup>Source: [https://www.who.int/csr/sars/country/table2004\\_04\\_21/en/](https://www.who.int/csr/sars/country/table2004_04_21/en/),

<sup>b</sup>Source: <https://www.who.int/emergencies/mers-cov/en/>

<sup>c</sup>Source: Situation report 55, 15 March 2020. [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200315-sitrep-55-covid-19.pdf?sfvrsn=33daa5cb\\_6](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200315-sitrep-55-covid-19.pdf?sfvrsn=33daa5cb_6)

None of the animals developed clinical signs or lesions. Virus isolation was unsuccessful; RNA was detected in blood from pigs and chickens and virus-neutralizing antibodies were detected in two pigs. The authors concluded that chickens and pigs likely do not play a role in virus amplification.<sup>25</sup> Recognized natural hosts of MERS-CoV include dromedaries and camels.<sup>26,27</sup> To further investigate the potential of other species to amplify MERS-CoV, llamas, pigs, sheep, and horses were experimentally infected.<sup>28</sup> Specifically, these species received MERS-CoV intranasally using a mucosal atomization device. Nasal and rectal swabs were collected over time, and MERS-CoV RNA and antigen and virus could be detected in nasal swabs from llamas and pigs. The authors concluded that MERS-CoV circulation in animals other than dromedaries, such as llamas and pigs, is not negligible.<sup>28</sup>

From the obtained data available today, it would appear pigs can carry SARS-CoV and develop antibodies. Furthermore, evidence exists that pigs can amplify MERS-CoV. So far there is no evidence that pigs can become infected with SARS-CoV-2 or are capable to amplify the virus. However, as the SARS-CoV-2 outbreak has just emerged and is ongoing any testing currently focuses on identifying infected people to prevent further human-to-human transmissions. Notably, it was reported that SARS-CoV-2 could use angiotensin-converting enzyme 2 (ACE2) from four animal species including porcine ACE2 as the receptor to enter the cell *in vitro*,<sup>29</sup> possibly suggesting that pigs may be susceptible to SARS-CoV-2 infection.

Theoretically, if pigs can be infected with SARS-CoV-2 and also amplify it, the virus would likely be present in the respiratory tract

of pigs so lungs or nasal swabs would need to be tested. In human CoV studies, it has been shown that RNA can be detected by PCR in serum or plasma obtained from patients with SARS-CoV, MERS-CoV, and also SARS-CoV-2 infections.<sup>30</sup> In addition, SARS-CoV-2 RNA was also detected in a patient's stool sample.<sup>31</sup> It is presently unknown if these events resemble just leakage of viral particles or fragments or if the virus can replicate outside the respiratory tract.<sup>30</sup> The risk associated with human blood for transmission to other people is unknown, but blood donations are not practiced in high-risk areas where infections are ongoing and it is recommended to measure the body temperature of blood donors prior to blood donation.

Interspecies transmission from humans to other species including pigs likely requires a close contact with infected people. A dog from Tai Hang, Islands District, Hong Kong, living in the same household as a confirmed COVID-19 patient was found SARS-CoV-2 RT-PCR positive on nasal swab and oral samples without showing any clinical signs beginning of February 2020 (Source: [https://www.oie.int/wahis\\_2/public/wahid.php/Reviewreport/Review?page\\_refer=MapFullEventReport&reportid=33455](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport/Review?page_refer=MapFullEventReport&reportid=33455)). While most pets often have close very contact to their owner, the situation with pigs is different. In China, the origin of SARS-CoV-2, where most infections in humans have been reported as of now, pig caretakers must be free of signs for COVID-19 before being allowed to enter pig farms, as one part of the national large-scale quarantine policy (Source: <https://necsi.edu/the-effect-of-travel-restrictions-on-the-domestic-spread-of-the-wuhan-coronavirus-2019-ncov>). Furthermore, viral spillovers from

one species into another species are further promoted by high mutation rates allowing the virus to overcome host-specific defenses. From sequences currently available on SARS-CoV-2, the mutation rate does not appear to be high (Source: <https://nextstrain.org/groups/ncov/sars-like-cov>). Based on today's knowledge, the risk of acquiring a SARS-CoV-2 infection while undergoing a transplantation procedure using porcine-derived materials should be considered low but likely needs to be properly assessed. Until this is the case, donor pigs can simply be tested by PCR for the presence of SARS-CoV-2 viral RNA or once available by serology for antibodies to further rule out any infection. This practice is currently already in place for human blood donors in Wuhan and Hubei Province in China.<sup>30</sup>

In summary, SARS-CoV-2 is emerging and spreading at a high rate in the human population. Due to the large number of infected people often with high virus loads, SARS-CoV-2 could potentially spill over in other species including pigs and this should be monitored closely. Evidence from SARS-CoV would suggest that it is likely to detect SARS-CoV-2 RNA in pigs but perhaps unlikely that the virus would be amplified in pigs.

## REFERENCES

- 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.
- De Groot RJ, Baker SC, Baric R, et al. Family Coronaviridae, p 806–828. In: King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ, eds. *Virus Taxonomy Ninth Report of the International Committee on Taxonomy of Viruses*. Amsterdam: Elsevier Academic Press; 2012.
- Bucknall RA, King LM, Kapikian AZ, Chanock RM. Studies with human coronaviruses. II. Some properties of strains 229E and OC43. *Proc Soc Exp Biol Med*. 1972;139:722-727.
- van der Hoek L, Pyrc K, Jebbink MF, et al. Identification of a new human coronavirus. *Nat Med*. 2004;10:368-373.
- Bruckova M, McIntosh K, Kapikian AZ, Chanock RM. The adaptation of two human coronavirus strains (OC38 and OC43) to growth in cell monolayers. *Proc Soc Exp Biol Med*. 1970;135:431-435.
- Woo PC, Lau SK, Chu CM, et al. Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia. *J Virol*. 2005;79:884-895.
- Drosten C, Preiser W, Gunther S, Schmitz H, Doerr HW. Severe acute respiratory syndrome: identification of the etiological agent. *Trends Mol Med*. 2003;9:325-327.
- Fouchier RA, Kuiken T, Schutten M, et al. Aetiology: Koch's postulates fulfilled for SARS virus. *Nature*. 2003;423:240.
- Ksiazek TG, Erdman D, Goldsmith CS et al., SARS Working Group. A novel coronavirus associated with severe acute respiratory syndrome. *N. Engl. J. Med*. 2003;348:1953-1966.
- Donnelly CA, Fisher MC, Fraser C, et al. Epidemiological and genetic analysis of severe acute respiratory syndrome. *Lancet Infect Dis*. 2004;4:672-683.
- Liang WN, Zhao T, Liu ZJ, et al. Severe acute respiratory syndrome—retrospect and lessons of 2004 outbreak in China. *Biomed Environ Sci*. 2006;19:445-451.
- Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med*. 2012;367:1814-1820.
- Gorbalenya AE, Baker SC, Baric RS, et al. (2020). The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol* <https://doi.org/10.1038/s41564-020-0695-z>
- Lu G, Wang Q, Gao GF. Bat-to-human: spike features determining 'host jump' of coronaviruses SARS-CoV, MERS-CoV, and beyond. *Trends Microbiol*. 2015;23(8):468-478.
- Lee KM. Propagation of transmissible gastroenteritis virus in tissue culture. *Ann N Y Acad Sci*. 1956;66:191-195.
- Pensaert MB, de Bouck P. A new coronavirus-like particle associated with diarrhea in swine. *Arch Virol*. 1978;58:243-247.
- Pensaert M, Callebaut P, Vergote J. Isolation of a porcine respiratory, non-enteric coronavirus related to transmissible gastroenteritis. *Vet Q*. 1986;8:257-261.
- Pan Y, Tian X, Qin P, et al. Discovery of a novel swine enteric alphacoronavirus (SeACoV) in southern China. *Vet Microbiol*. 2017;211:15-21.
- Zhou P, Fan H, Lan T, et al. Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. *Nature*. 2018;556:255-258.
- Greig AS, Mitchell D, Corner AH, Bannister GL, Meads EB, Julian RJ. A hemagglutinating virus producing encephalomyelitis in baby pigs. *Can J Comp Med Vet Sci*. 1962;26:49-56.
- Woo PC, Lau SK, Lam CS, et al. Discovery of seven novel Mammalian and avian coronaviruses in the genus deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus. *J Virol*. 2012;86:3995-4008.
- Halbur PG, Paul PS, Vaughn EM, Andrews JJ. Experimental reproduction of pneumonia in gnotobiotic pigs with porcine respiratory coronavirus isolate AR310. *J Vet Diagn Invest*. 1993;5:184-188.
- Lanza I, Brown IH, Paton DJ. Pathogenicity of concurrent infection of pigs with porcine respiratory coronavirus and swine influenza virus. *Res Vet Sci*. 1992;53:309-314.
- Chen W, Yan M, Yang L, et al. SARS-associated coronavirus transmitted from human to pig. *Emerg Infect Dis*. 2005;11:446-448.
- Weingartl HM, Copps J, Drebot MA, et al. Susceptibility of pigs and chickens to SARS coronavirus. *Emerg Infect Dis*. 2004;10:179-184.
- Wernery U, Lau SK, Woo PC. Middle East respiratory syndrome (MERS) coronavirus and dromedaries. *Vet J*. 2017;220:75-79.
- Farag E, Sikkema RS, Mohamedani AA, et al. MERS-CoV in camels but not camel handlers, Sudan, 2015 and 2017. *Emerg Infect Dis*. 2019;25:2333-2335.
- Vergara-Alert J, van den Brand JM, Widagdo W, et al. Livestock susceptibility to infection with middle east respiratory syndrome coronavirus. *Emerg Infect Dis*. 2017;23:232-240.
- 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.
- Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. *Transfus Med Rev*. 2020. <https://doi.org/10.1016/j.tmr.2020.02.003>. [Epub ahead of print].
- Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020;382(10):929-936.