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CORONAVIRUS DISEASE 2019 UPDATE (400): ANIMAL, SHEEP, RESEARCH, EXPERIMENTAL INFECTION

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<https://www.biorxiv.org/content/10.1101/2021.11.15.468720v1.full.pdf>

Citation: Gaudreault NN, Cool K, Trujillo JD, Morozov I, et al. Susceptibility of sheep to experimental co-infection with the ancestral lineage of SARS-CoV-2 and its alpha variant. bioRxiv preprint doi: <https://doi.org/10.1101/2021.11.15.468720>, [this version posted 17 Nov 2021].

#### Abstract

SARS-CoV-2 is highly transmissible and the cause of coronavirus disease 2019 (COVID-19) in humans. A wide range of animal species have also been shown to be susceptible to SARS-CoV-2 infection by experimental and/or natural infections. Domestic and large cats, mink, ferrets, hamsters, deer-mice, white-tailed deer, and non-human primates have been shown to be highly susceptible, whereas other species such as mice, dogs, pigs, and cattle appear to be refractory to infection or have very limited susceptibility. Sheep (*Ovis aries*) are a commonly farmed domestic ruminant that have not previously been thoroughly investigated for their susceptibility to SARS-CoV-2.

We performed in vitro and in vivo studies which consisted of infection of ruminant-derived cell cultures and experimental challenge of sheep to investigate their susceptibility to SARS-CoV-2. Our results showed that sheep-derived cell cultures support SARS-CoV-2 replication. Furthermore, experimental challenge of sheep demonstrated limited infection with viral RNA shed in nasal and oral swabs primarily at 1-day post challenge (DPC), and also detected in the respiratory tract and lymphoid tissues at 4 and 8 DPC. Sero-reactivity was also observed in some of the principal infected sheep but not the contact sentinels, indicating that transmission to co-mingled naïve sheep was not highly efficient; however, viral RNA was detected in some of the respiratory tract tissues of sentinel animals at 21 DPC. Furthermore, we used challenge inoculum consisting of a mixture of two SARS-CoV-2 isolates, representatives of the ancestral lineage A and the B.1.1.7-like alpha variant of concern (VOC), to study the competition of the 2 virus strains.

Our results indicate that sheep show low susceptibility to SARS-CoV-2 infection, and that the alpha VOC outcompeted the ancestral lineage A strain.

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[The trial involved 10 male sheep, approximately 6 months of age. It was performed in the biosafety level-3+ and BSL-3Ag laboratories and facilities in the Biosecurity Research Institute at KSU in Manhattan, KS, USA. (<https://www.bri.k-state.edu/research/bsl-3ag.html>).

On the day of challenge, 8 'principal infected sheep' (PIS) were inoculated with a 1:10 titer ratio of lineage A WA1 and the alpha VOC B.1.1.7 strains. A 2 ml dose of  $1 \times 10^6$  TCID<sub>50</sub> per animal was administered through intra-nasal and oral routes, simultaneously. The remaining 2 non-infected (naive) sheep were co-mingled with the challenged animals at 1 day-post-challenge (DPC) as contact sentinels for the duration of the study. A subset of the PIS were euthanized and postmortem examination was performed at 4 (n = 3) and 8 (n = 3) DPC. Postmortem examination of the remaining 2 PIS and 2 sentinel sheep was performed at 21 DPC.

None of the 8 PIC became febrile after challenge or during the 21-day study; no other obvious clinical signs were observed in any of them, nor in the 2 sentinel sheep, during the study: no weight loss, lethargy, diarrhea, inappetence, or respiratory distress.

The authors conclude: "our results demonstrate that experimental challenge of sheep with SARSCoV-2 results in a limited subclinical infection, and while transmission to naive co-mingled sheep appeared to occur, it did not lead to highly productive infection; therefore, domestic sheep are unlikely to be amplifying hosts for SARS-CoV-2. Based on our results and the currently available published data, further investigations into SARS-CoV-2 infection in sheep and other ruminant species are warranted. The identification of additional susceptible hosts provides critical information for SARS-CoV-2 epidemiology, in order to establish surveillance protocols, and to improve our mitigation strategies and preventative measures at the human-animal interface".

An animal-to-human COVID-19 infection has, so far, been seen only on mink farms (Denmark), where a mink-associated variant of the COVID-19 virus was the outcome of the transmission of the virus from humans to minks, followed by mink-to-mink and back to human infections. Among other kept animal species, infected from humans, only cats and ferrets transmitted the virus intra-species; no animal-to-human (zoonotic) infections, by these species, has been recorded. OIE and WHO have published guidelines for those engaged in mink farming, pertaining to specified biosecurity measures for the prevention of human exposure. - Mod.AS]

## See Also

COVID-19 update (29): animal, peridomestic wildlife, experimental infection 20210122.8126905

COVID-19 update (20): animal, deer, experimental infection 20210116.8108967

2020

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COVID-19 update (551): animal, pig, research, experimental infection 20201223.8041877

COVID-19 update (530): animal, mink, research, experimental infection, vaccine 20201210.8009205

COVID-19 update (450): animal, cattle, research, experimental infection 20201022.7883213

COVID-19 update (448): animal, raccoon dog, research, experimental infection 20201022.7880283

COVID-19 update (345): animal, cat, research, experimental infection 20200805.7648370

COVID-19 update (227): animal, cat, dog, research, experimental infection 20200601.7416648

COVID-19 update (183): Japan/USA, animal, research, cat, experimental infection 20200514.7337185

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