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Animal models of SARS-CoV-2 transmission

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SARS-CoV-2 emerged in China as a zoonotic virus in December 2019. The virus proved to be human-to-human transmissible and its global spread resulted in the ongoing COVID-19 pandemic, associated with high morbidity and mortality. Vaccines were developed at an unprecedented speed and proved to be efficacious in preventing disease, but it remains to be determined if vaccines are able to interrupt transmission. Moreover, virus variants of concern continue to emerge that appear more transmissible and/or less sensitive to virus-specific immune responses. Here, we briefly review the role of animal models in assessing prophylactic and therapeutic options to interrupt SARS-CoV-2 transmission.

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Introduction

In December 2019 a cluster of patients with severe respiratory tract disease was notified in Wuhan, China. A novel coronavirus was rapidly identified as the causative agent and due to the close relationship to severe acute respiratory syndrome (SARS)-coronavirus the virus was named SARS-CoV-2 [1]. Efficient transmission, even by pre-symptomatic and asymptomatic individuals, combined with domestic and international travel, resulted in a pandemic of coronavirus disease-2019 (COVID-19). Phylogenetic comparison with previously identified coronaviruses suggested a zoonotic origin of SARS-CoV-2 [2–4]. A wide diversity of closely related betacoronaviruses was detected in bats and pangolins across Asia [5,6,7••], but the exact source species and potential intermediate host remain elusive.

Human-to-human transmission

Since the majority of COVID-19 outbreaks occurred in household settings or events involving clusters of people in close contact, it is thought that SARS-CoV-2 is primarily transmitted via direct, indirect or close contact with infected individuals through contaminated secretions like saliva, respiratory droplets and aerosols. These droplets and aerosols can be expelled by coughing, sneezing, talking or singing and infect the subsequent host by reaching the respiratory tract or eyes [8–14]. Evidence for long-distance airborne transmission between humans is limited [15]. Despite consistent evidence that SARS-CoV-2 can survive on specific surfaces [16–18,19•], evidence of fomite transmission between humans is also limited. In addition to respiratory transmission, viable SARS-CoV-2 has been demonstrated in urine [20] and stool specimens [21,22] obtained from infected humans, but transmission via the fecal-oral route is thought to be of limited relevance in the spread of the virus among humans.

SARS-CoV-2 RNA can be detected by RT-PCR on nasopharyngeal swab material 1–3 days before symptom onset, with peak values around symptom onset, followed by a gradual decline over time [23–27]. Persistence of RNA for several weeks has been reported, especially in individuals with severe COVID-19 [23,24,28,29]. However, detection of infectious virus is a better measure for transmissibility [30••]. Shedding of infectious virus was initially not thought to occur for more than 8 days after symptom onset [24,31,32], but a recent study showed longer shedding of infectious virus in a selection of patients, which positively correlated with disease severity and viral load. In that study, infectious virus shedding became undetectable with the appearance of neutralizing antibodies in serum [30••]. Comparative studies have shown that the relationship between detection of viral RNA and infectiousness differs between persons with mild and severe disease [33]. The level of shedding of viral RNA differs greatly among individuals, in part explaining the observed highly skewed patterns of transmission towards a limited proportion of human-to-human contacts [34].

Transmission by individuals without symptoms was already suspected early in the pandemic. Two transmission 'types' can be distinguished: transmission by asymptomatic (infected people who never develop symptoms) or by pre-symptomatic (infected people who have not yet developed symptoms) individuals. The true extent of

asymptomatic infections is still unclear, but a recent systematic review and meta-analysis (that included several studies with limitations) estimated the proportion of truly asymptomatic cases to be 1 in 6 infections [35]. A study performed in close contacts of confirmed COVID-19 cases estimated the proportion to be 23% [36]. Both studies demonstrated transmission by asymptomatic individuals, albeit it to a lower extent compared to transmission by symptomatic patients. Pre-symptomatic transmission has often been demonstrated, and is in line with isolation of infectious virus as discussed above. Although frequently demonstrated, the estimated rates of pre-symptomatic transmission vary considerably: from 6.4% up to 44% [25,37,38]. Clearly such parameters are not fixed and may differ for emerging variants with increased transmissibility and/or disease severity.

Emergence of other zoonotic coronaviruses

Two other zoonotic coronaviruses recently emerged to cause outbreaks in humans. In 2003 SARS-coronavirus emerged from bats [39,40], most likely via infection of palm civets as intermediate host [41]. SARS-CoV caused a large outbreak that was initiated by several superspreading events and subsequently amplified in hospitals [42]. The outbreak was associated with high case-fatality rates. However, in contrast to SARS-CoV-2, SARS-CoV proved to be only moderately transmissible among humans. This was probably due to the fact that viral excretion peaked relatively late, around 10 days post symptoms onset [43–45], leading to a predominant occurrence of transmission in the second week of illness. At this stage infectious patients were often hospitalized and most cases of SARS-CoV human-to-human transmission occurred in healthcare settings, potentially due to aerosol-generating procedures. Transmission by pre- or asymptomatic individuals (as described above for SARS-CoV-2) proved to be limited [46]. This strongly facilitated case-based surveillance, contract tracing and isolation measures. Although SARS-CoV was spread to multiple countries, the outbreak was fully contained by non-pharmaceutical interventions [47,48].

In 2012 another zoonotic coronavirus was identified as the causative agent of a cluster of severe respiratory tract disease patients in the Middle East and was named Middle East Respiratory Syndrome (MERS)-coronavirus [49]. Dromedary camels were identified as intermediate host [50,51] and it is thought that the virus likely originated from bats (similar to SARS-CoV and SARS-CoV-2) [49,52]. Although MERS-CoV rapidly spread globally [53], it is generally regarded less human-to-human transmissible than SARS-CoV or SARS-CoV-2, with an early estimate of an R_0 below 1 in the general community and in households [54•]. In healthcare settings human-to-human transmission has led to large outbreaks with higher R_0, providing a warning sign for pandemic potential [55–57]. Continuous zoonotic events are being reported. The current consensus is that close and prolonged contact with an index case seems to be required for MERS-CoV transmission and adaptation would be required for efficient human-to-human transmission.

COVID-19 outbreak containment

Strategies to contain the COVID-19 pandemic were initially limited to non-pharmaceutical interventions, including lockdowns and physical distancing measures. Within a year after onset of the pandemic, several vaccines were developed and shown to be safe and effective in large double-blind placebo-controlled clinical studies [58••,59••,60••,61••]. Large-scale implementation of these vaccines will reduce morbidity and mortality, alleviate the pressure on health care systems and relieve non-pharmaceutical interventions. However, it remains unclear how well vaccines protect from upper respiratory tract shedding and subsequent viral transmission. A recent study found the first evidence of reduced incidence of infection in household contacts of vaccinated healthcare workers, but the level of protection from shedding may differ for different variants, with age, and with time since vaccination [62]. In addition, it remains to be determined what vaccination coverage will be reached eventually, given vaccine hesitancy and disparities in access. Therefore, for the months and years ahead, it is crucial to continue to explore potential additional countermeasures that inhibit SARS-CoV-2 transmission.

Animal models to study coronavirus transmission

Animal models have been instrumental to gain insight into SARS-CoV, MERS-CoV and SARS-CoV-2 replication kinetics, shedding, pathogenesis and medical countermeasures, and have been reviewed elsewhere [63•,64–66]. These models include non-human primates (NHPs), cats, dromedary camels, ferrets, hamsters, rabbits and (transgenic) mice. Since coronaviruses emerge after zoonotic introduction, it is essential to study coronavirus transmission potential and evaluate transmission prevention by medical countermeasures. Animal models of transmission are therefore crucial. For SARS-CoV-2 specifically, this includes assessment of transmissibility of emerging variants, or transmission in the presence of vaccine-induced immunity. In this review, we provide a brief summary of the currently employed animal models to study different aspects of COVID-19, with a focus on transmission in combination with therapeutics that could interrupt transmission.

Transmission studies in animal models are relatively scarce. Natural SARS-CoV-2 transmission in animals has been described in companion animals (e.g. cats and dogs) and on mink farms. Experimental animal transmission models remain limited to the cat, ferret and hamster model. Although it has been shown that rabbits are susceptible to experimental SARS-CoV-2 infection, given

Table 1

Overview of transmission models

	Mouse	Cat	Hamster	Ferret	Fruit bat	NHP[d]
Animal handling BSL3	Easy	Difficult	Easy	Intermediate	Difficult	Difficult
Species relevance	Limited	Limited	Limited	Sialic acids RT[a] resemble human	Close to original host	Close to human
Naturally susceptible	Only variants[b]	Yes	Yes	Yes	Not fully	Yes
Clinical presentation	Variable	Limited disease	Severe disease	Limited disease	Limited disease	Limited disease
Transmission efficacy[c]	Unknown	DC: efficient Aer: not efficient	DC: efficient Aer: efficient	DC: efficient Aer: possible	Limited	Unknown
Reagents availability	Widespread	Limited	Limited	Limited	Limited	Widespread
Transmission literature	Not available	Limited	Multiple publications	Multiple publications	Limited	Not available
References	N/A	[74,76,77]	[97••,104,108]	[87,89,91,94••]	[89]	N/A

[a] RT = respiratory tract.
[b] mouse susceptibility differs per model, dependent on the use of mouse strain / transgenic mice. Some models are susceptible to variants of concern [63•,117].
[c] DC = direct contact, aer = aerosol.
[d] NHP = non-human primates.

the high dose needed to establish productive infection, transmission of the virus from rabbit-to-rabbit is unlikely [67]. Ferrets thus far appear an ideal model to study transmission in the absence of clinical signs, whereas hamsters are more appropriate to study transmission in the context of pathology and severe disease. NHPs are rarely used for transmission studies, in part due to practical limitations in high-containment facilities. An overview of the characteristics of different animal models and their usability in transmission studies is shown in Table 1.

Human-to-animal transmission: companion animals

Naturally occurring human-to-animal transmission was already reported during the SARS-CoV outbreak in 2002/2003. Viral RNA was detected in oropharyngeal swabs obtained from cats after contact with infected individuals, and infections were confirmed serologically [68]. Susceptibility of cats was subsequently confirmed experimentally [69]. Because of these reports, several studies performed in Hong Kong describe swabbing of companion animals in close contact with confirmed COVID-19 cases. Here, household transmission to dogs [70] and cats [71] was observed, but in most cases infected animals remained asymptomatic [72]. This remains to be determined for emerging variants [73]. Experimental infections confirmed susceptibility of cats, but dogs proved poorly susceptible [74,75].

Cats were also evaluated as an animal model for SARS-CoV-2 transmission. A first study assessed airborne transmission among cats housed in adjacent cages (also allowing for respiratory droplet transmission) and demonstrated that experimental transmission is feasible, although this remained limited to infection of 1 out of 3 sentinel animals [75]. Direct contact transmission in cats was more robust, showing infection of all sentinel animals in several separate small studies [74,76,77].

Human-to-animal transmission: outbreaks on mink farms

Large outbreaks of SARS-CoV-2 infection have been reported on mink (*Neovison vison*) farms in the Netherlands, Spain, Italy, Sweden, Greece, the US and Denmark, initiated by a human-to-mink transmission [78]. Circulation and spread initially went unnoticed as mustelids usually develop asymptomatic or mild disease, and transmission on some farms was only confirmed after serological surveys. However, upper and lower respiratory tract involvement has been described [79,80]. Transmission on mink farms was rapid and widespread after initial introduction. Once introduced, it has proven difficult to stop transmission on a farm, and ongoing transmission between farms was described [81•]. Large-scale culling of mink was initiated when it was observed that ongoing SARS-CoV-2 transmission led to an accumulation of mutations in the S protein, and that these viruses could spill back from mink farms into the community in Denmark and possibly the Netherlands [81•,82–84].

Experimental infection or transmission studies in mink have not been performed to date. Mink belong to the family of mustelids (*Mustelidae*), together with ferrets. Ferrets were already shown to be highly susceptible to SARS-CoV in 2003 [69], and are now in widespread use to study SARS-CoV-2 transmission and pathogenesis.

Experimental SARS-CoV-2 transmission studies: ferrets

Ferrets (*Mustela putorius furo*) are an invaluable model to study the pathogenicity and transmission of respiratory viruses [85]. In SARS-CoV-2 infection studies, it was shown that ferrets rarely develop clinical signs of disease. Weight loss is not observed, some studies report a slight and transient fever. Additionally, mild respiratory symptoms (e.g. nasal discharge) and mild haematological changes (e.g. lymphopenia) have occasionally been reported [75,86–89]. However, although clinical symptoms are absent or mild, there is substantial shedding of SARS-CoV-2 observed in the respiratory tract, starting at day 2 and sometimes still detectable by RT-PCR two weeks post inoculation [87,90•,91]. Since ferrets develop no or relatively mild disease and histopathological changes, combined with RT-PCR detectable viral loads and shedding from the respiratory tract, ferrets are regarded an optimal model for asymptomatic or mild disease in humans and are often used in transmission studies [92]. Recently, it was shown that aged ferret (>3 years old) have higher viral loads, longer shedding and more severe lung inflammatory cell infiltration, accompanied by more clinical symptoms (fever and weight loss) compared to juvenile and young adult ferrets [93].

SARS-CoV-2 transmission via direct contact was found to be the most efficient route of transmission, since all naive contact animals became infected during co-housing in different transmission studies [87,89,91]. SARS-CoV-2 transmission via the air over short distance (i.e. animals were separated by a maximum distance of 10 cm) occurred in two out of six [87] and three out of four animals [91], whereas transmission via the air over more than one meter distance occurred in two out of four ferret pairs [94••]. Despite the similarities in transmission efficiencies between the studies, differences were observed in the robustness of infection of recipient animals and the time after exposure that animals became infected. Whereas in most studies infection by either route resulted in a similar duration and level of virus shedding in (in) direct recipient animals as compared to the donor animals [89,91,94••], Kim *et al.* detected only low levels of SARS-CoV-2 RNA in nasal washes of the indirect recipient ferrets, virus shedding was shorter and no infectious virus was isolated [87].

Because of efficient SARS-CoV-2 direct contact transmission, ferrets are a sensitive model to evaluate prophylactic and therapeutic intervention strategies aimed at preventing virus transmission. As such, the model was used to demonstrate that prophylactic daily intranasal administration of a stable fusion inhibitory lipopeptide, which interacts with the HRN region of S_2 and prevents conformational changes in the S protein, could completely prevent SARS-CoV-2 direct contact transmission during 24-hour co-housing with infected animals [90•]. In another study, a ribonucleoside analogue inhibitor initially intended as influenza treatment (MK-4482/EIDD-2801) was evaluated in the ferret model as a therapeutic treatment. Treatment with orally administered MK-4482/EIDD-2801, twice a day, significantly reduced the SARS-CoV-2 load in the upper respiratory tract of ferrets and prevented transmission to untreated contact animals that were exposed 30 hours after inoculation of donors [95•].

Experimental SARS-CoV-2 transmission studies: hamsters

Molecular docking studies on the binding between Ace2 and the S protein initially suggested that the Syrian golden hamster (*Mesocricetus auratus*) is a suitable small animal model for SARS-CoV-2 pathogenesis studies [96,97••]. Indeed, upon intranasal challenge hamsters develop acute but transient respiratory distress, peaking at 4–5 days post inoculation, and lose weight, followed by an eventual recovery [96,97••,98]. SARS-CoV-2 infection of hamsters is associated with high viral loads and prolonged detection of viral genomes in oral swabs and nasal washes by RT-PCR. Hamsters additionally show clear histopathological lesions [96,98,99]. Upon comparison of the course of SARS-CoV-2 infection in young and aged hamsters, it was found that replication kinetics are similar but aged hamsters exhibit more pronounced weight loss, combined with more histopathological lung damage [100]. Because hamsters recapitulate (part of) COVID-19 disease as observed in humans and they are a relatively easy to handle, hamsters are a valuable model to study severe COVID-19 in humans. Furthermore, hamsters can be used to screen antiviral agents in a disease model [101]. Finally, hamsters have been used in adoptive transfer and vaccination challenge studies [102,103].

Although viral RNA can persist in the hamster respiratory tract, infectious virus can be detected only for a short period after intranasal inoculation, leaving a potentially small window for transmission. However, transmission of SARS-CoV-2 to naive animals that were co-housed with infected animals in a direct contact setup is robust [96,97••,104]. It was determined that the minimal amount of contact time between infected and naive hamsters required for efficient transmission is 4 hours [105] or less [97••]. In addition, despite the prolonged detection of viral RNA in nasal washes and throat swabs for over two weeks, transmission only occurs during the first six days post inoculation [97••]. Aerosol transmission models for hamsters have also been developed, are robust, and more efficient than fomite transmission [97••,104]. Interestingly, hamsters infected through direct contact transmission develop no or only limited weight loss, in contrast to directly inoculated animals.

Prior exposure of hamsters to SARS-CoV-2 resulted in protection from re-infection, with significantly reduced virus replication in the upper respiratory tract [106]. Virus

was not transmitted to naive contact animals, suggesting that natural immunity to SARS-CoV-2 can prevent transmission. However, to date, immunity induced by most vaccine candidates or passive transfer of neutralizing antibodies can only effectively protect against respiratory disease in the lower respiratory tract, but not in the nose [96,98,105,107]. The hamster model has also been used to evaluate the efficacy of non-medical intervention strategies, such as surgical masks. In a single study, SARS-CoV-2 could be transmitted by respiratory droplets or airborne droplet nuclei which could be reduced by a surgical mask partition between infected and naive hamsters [108].

Finally, most hamster transmission studies have focused on respiratory transmission; however, other routes of transmission may occur. Especially in direct contact set-ups, concerns of fecal-oral transmission have been raised given that hamsters can be infected via the oral route and SARS-CoV-2 shedding has been detected in feces of experimentally infected animals [109].

Conclusions

In conclusion, SARS-CoV-2 transmission and transmission intervention studies in animal models remain scarce and have mostly been performed with the classical variant of SARS-CoV-2. Zhou *et al.* addressed the transmissibility of the predominant circulating variant (D614G) [110] in the hamster and ferret model, in a pairwise competition setup in 6 animal pairings, and observed increased transmission of the variant [111]. Future studies will need to address differences in transmissibility of novel emerging variants of concern, for which epidemiological studies have demonstrated potential increased transmissibility in humans. Another aspect that future transmission studies will need to take into account is the age of animals. COVID-19 is most severe in the elderly (with underlying co-morbidities) [3], but transmission studies so far do not take age into account. In pathogenesis studies it was shown that SARS-CoV-2 causes more severe disease in aged hamsters, ferrets, and non-human primates [112,113]. Similar observations were reported for experimental infections with SARS-CoV [114]. The influence of gender of experimental animals in transmission studies is still unknown.

Several potential pitfalls should be taken into account when performing these studies: (1) adequate production and characterization of non-adapted viral stocks with a representative viral sequence [115], (2) potential variations in route, dose and inoculation volume in experimental set-ups, (3) in-host adaptation of the virus (however, studies in immunocompromised animals may allow assessment of in-host adaptation, such as previously demonstrated in humans [116]), and (4) the development of standardized protocols to quantitatively assess transmission efficacy in animals, while respecting 3R policies in animal research. Especially transmission efficacy is now addressed and compared in small studies (mostly with a handful of animals), with limited statistical power or results that could be quantitively assessed. Performing *in vivo* competition experiments is a potential alternative.

Only few studies have assessed prevention of SARS-CoV-2 transmission by antibodies or antiviral compounds. When studying the effectiveness of candidate intervention strategies, this should be studied both at level of the infected host (therapeutic efficacy, e.g. nucleoside analogues) and at the level of the recipient (prophylactic efficacy, e.g. fusion inhibitory lipopeptides). Moreover, animal models may allow assessment of the potential added benefit of combination therapy using antiviral compounds with different working mechanisms.

In conclusion, mitigation of SARS-CoV-2 transmission will be crucial to contain the ongoing COVID-19 pandemic. This will likely require a combination of non-pharmaceutical interventions, increased vaccination coverage and potentially antivirals that reduce virus loads or prevent virus entry. Transmission studies in animal models may support pre-clinical identification of promising intervention strategies for further clinical testing.

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Conflict of interest statement

Nothing declared.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Coronaviridae Study Group of the International Committee on Taxonomy of Virsus: **The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2**. *Nat Microbiol* 2020, **5**:536-544.

2. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF: **The proximal origin of SARS-CoV-2**. *Nat Med* 2020, **26**:450-452.

3. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY *et al.*: **A new coronavirus associated with human respiratory disease in China**. *Nature* 2020, **579**:265-269.

4. Zhang YZ, Holmes EC: **A genomic perspective on the origin and emergence of SARS-CoV-2**. *Cell* 2020, **181**:223-227.

5. Lam TT, Jia N, Zhang YW, Shum MH, Jiang JF, Zhu HC, Tong YG, Shi YX, Ni XB, Liao YS *et al.*: **Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins**. *Nature* 2020, **583**:282-285.

6. Xiao K, Zhai J, Feng Y, Zhou N, Zhang X, Zou JJ, Li N, Guo Y, Li X, Shen X *et al.*: **Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins**. *Nature* 2020, **583**:286-289.

7. •• Zhou H, Ji J, Chen X, Bi Y, Li J, Hu T, Song H, Chen Y, Cui M, Zhang Y *et al.*: **Identification of novel bat coronaviruses sheds light on the evolutionary origins of SARS-CoV-2 and related viruses**. *bioRxiv* 2021

This study describes the high diversity of coronaviruses in South-East Asian bat species, including close relatives of SARS-CoV and SARS-CoV-2.

8. Barnett BP, Wahlin K, Krawczyk M, Spencer D, Welsbie D, Afshari N, Chao D: **Potential of ocular transmission of SARS-CoV-2: a review**. *Vision (Basel)* 2020, **4**:40.

9. Deng W, Bao L, Gao H, Xiang Z, Qu Y, Song Z, Gong S, Liu J, Liu J, Yu P *et al.*: **Ocular conjunctival inoculation of SARS-CoV-2 can cause mild COVID-19 in rhesus macaques**. *Nat Commun* 2020, **11**:4400.

10. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Yip CC, Poon RW *et al.*: **A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster**. *Lancet* 2020, **395**:514-523.

11. Ghinai I, McPherson TD, Hunter JC, Kirking HL, Christiansen D, Joshi K, Rubin R, Morales-Estrada S, Black SR, Pacilli M *et al.*: **First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA**. *Lancet* 2020, **395**:1137-1144.

12. Hamner L, Dubbel P, Capron I, Ross A, Jordan A, Lee J, Lynn J, Ball A, Narwal S, Russell S *et al.*: **High SARS-CoV-2 attack rate following exposure at a choir practice – Skagit county, Washington, March 2020**. *MMWR Morb Mortal Wkly Rep* 2020, **69**:606-610.

13. Liu J, Liao X, Qian S, Yuan J, Wang F, Liu Y, Wang Z, Wang FS, Liu L, Zhang Z: **Community transmission of severe acute respiratory syndrome coronavirus 2, Shenzhen, China, 2020**. *Emerg Infect Dis* 2020, **26**:1320-1323.

14. Pung R, Chiew CJ, Young BE, Chin S, Chen MI, Clapham HE, Cook AR, Maurer-Stroh S, Toh M, Poh C *et al.*: **Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures**. *Lancet* 2020, **395**:1039-1046.

15. WHO: *Scientific Brief: Transmission of SARS-CoV-2: Implications for Infection Prevention Precautions*. www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions2020.

16. Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, Marimuthu K: **Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient**. *JAMA* 2020, **323**:1610-1612.

17. Pastorino B, Touret F, Gilles M, de Lamballerie X, Charrel RN: **Prolonged infectivity of SARS-CoV-2 in fomites**. *Emerg Infect Dis* 2020, **26**:2256.

18. Chia PY, Coleman KK, Tan YK, Ong SWX, Gum M, Lau SK, Lim XF, Lim AS, Sutjipto S, Lee PH *et al.*: **Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients**. *Nat Commun* 2020, **11**:2800.

19. • van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, Tamin A, Harcourt JL, Thornburg NJ, Gerber SI *et al.*: **Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1**. *N Engl J Med* 2020, **382**:1564-1567

Initial comparison of potential for aerosol and fomite transmission of SARS-CoV and SARS-CoV-2.

20. Sun J, Zhu A, Li H, Zheng K, Zhuang Z, Chen Z, Shi Y, Zhang Z, Chen SB, Liu X *et al.*: **Isolation of infectious SARS-CoV-2 from urine of a COVID-19 patient**. *Emerg Microbes Infect* 2020, **9**:991-993.

21. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, Tan W: **Detection of SARS-CoV-2 in different types of clinical specimens**. *JAMA* 2020, **323**:1843-1844.

22. Xiao F, Sun J, Xu Y, Li F, Huang X, Li H, Zhao J, Huang J, Zhao J: **Infectious SARS-CoV-2 in feces of patient with severe COVID-19**. *Emerg Infect Dis* 2020, **26**:1920-1922.

23. Pan Y, Zhang D, Yang P, Poon LLM, Wang Q: **Viral load of SARS-CoV-2 in clinical samples**. *Lancet Infect Dis* 2020, **20**:411-412.

24. Wolfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Muller MA, Niemeyer D, Jones TC, Vollmar P, Rothe C *et al.*: **Virological assessment of hospitalized patients with COVID-2019**. *Nature* 2020, **581**:465-469.

25. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, Lau YC, Wong JY, Guan Y, Tan X *et al.*: **Temporal dynamics in viral shedding and transmissibility of COVID-19**. *Nat Med* 2020, **26**:672-675.

26. To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, Yip CC, Cai JP, Chan JM, Chik TS *et al.*: **Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study**. *Lancet Infect Dis* 2020, **20**:565-574.

27. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, Yu J, Kang M, Song Y, Xia J *et al.*: **SARS-CoV-2 viral load in upper respiratory specimens of infected patients**. *N Engl J Med* 2020, **382**:1177-1179.

28. Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, Xu H: **Positive RT-PCR test results in patients recovered from COVID-19**. *JAMA* 2020, **323**:1502-1503.

29. Ling Y, Xu SB, Lin YX, Tian D, Zhu ZQ, Dai FH, Wu F, Song ZG, Huang W, Chen J *et al.*: **Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients**. *Chin Med J (Engl)* 2020, **133**:1039-1043.

30. •• van Kampen JJA, van de Vijver D, Fraaij PLA, Haagmans BL, Lamers MM, Okba N, van den Akker JPC, Endeman H, Gommers D, Cornelissen JJ *et al.*: **Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19)**. *Nat Commun* 2021, **12**:267

This study demonstrated that combined information on viral RNA load and serological status predicts transmissibility.

31. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, Boodman C, Bello A, Hedley A, Schiffman Z *et al.*: **Predicting infectious SARS-CoV-2 from diagnostic samples**. *Clin Infect Dis* 2020, **71**:2663-2666.

32. Liu WD, Chang SY, Wang JT, Tsai MJ, Hung CC, Hsu CL, Chang SC: **Prolonged virus shedding even after seroconversion in a patient with COVID-19**. *J Infect* 2020, **81**:318-356.

33. van Beek J, Igloi Z, Boelsums T, Fanoy E, Gotz H, Molenkamp R, van Kampen JJA, GeurtsvanKessel C, van der Eijk AA, van de Vijver DAMC *et al.*: **From more testing to smart testing: data-guided SARS-CoV-2 testing choices**. *medRxiv* 2020.

34. Chen PZ, Bobrovitz N, Premji Z, Koopmans M, Fisman DN, Gu FX: **Heterogeneity in transmissibility and shedding SARS-CoV-2 via droplets and aerosols**. *eLife* 2021, **10**:e65774.

35. Byambasuren Y, Cardona M, Bell K, Clark J, McLaws M, Glasziou P: **Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis**. *JAMMI* 2020, **5**:223-234.

36. Wang Y, He Y, Tong J, Qin Y, Xie T, Li J, Li J, Xiang J, Cui Y, Higgs ES *et al.*: **Characterization of an asymptomatic cohort of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected individuals outside of Wuhan, China**. *Clin Infect Dis* 2020, **71**:2132-2138.

37. Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ: **Presymptomatic transmission of SARS-CoV-2-Singapore, January 23-March 16, 2020**. *MMWR Morb Mortal Wkly Rep* 2020, **69**:411-415.

38. Yu P, Zhu J, Zhang Z, Han Y: **A familial cluster of infection associated with the 2019 novel coronavirus indicating possible person-to-person transmission during the incubation period**. *J Infect Dis* 2020, **221**:1757-1761.

39. Drosten C, Gunther S, Preiser W, van der Werf S, Brodt HR, Becker S, Rabenau H, Panning M, Kolesnikova L, Fouchier RA *et al.*: **Identification of a novel coronavirus in patients with severe acute respiratory syndrome**. *N Engl J Med* 2003, **348**:1967-1976.

40. Kuiken T, Fouchier RA, Schutten M, Rimmelzwaan GF, van Amerongen G, van Riel D, Laman JD, de Jong T, van Doornum G,

Lim W *et al.*: **Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome**. *Lancet* 2003, **362**:263-270.

41. Guan Y, Zheng BJ, He YQ, Liu XL, Zhuang ZX, Cheung CL, Luo SW, Li PH, Zhang LJ, Guan YJ *et al.*: **Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China**. *Science* 2003, **302**:276-278.

42. Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddad LJ, Hedley AJ, Leung GM, Ho LM, Lam TH, Thach TQ *et al.*: **Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions**. *Science* 2003, **300**:1961-1966.

43. Chan KH, Poon LL, Cheng VC, Guan Y, Hung IF, Kong J, Yam LY, Seto WH, Yuen KY, Peiris JS: **Detection of SARS coronavirus in patients with suspected SARS**. *Emerg Infect Dis* 2004, **10**:294-299.

44. Hung IF, Cheng VC, Wu AK, Tang BS, Chan KH, Chu CM, Wong MM, Hui WT, Poon LL, Tse DM *et al.*: **Viral loads in clinical specimens and SARS manifestations**. *Emerg Infect Dis* 2004, **10**:1550-1557.

45. Peiris JS, Chu CM, Cheng VC, Chan KS, Hung IF, Poon LL, Law KI, Tang BS, Hon TY, Chan CS *et al.*: **Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study**. *Lancet* 2003, **361**:1767-1772.

46. Lee CC, Chen SY, Chang IJ, Tsai PC, Lu TC, Wu PL, Chen WJ, Huang LM, Chang SC: **Seroprevalence of SARS coronavirus antibody in household contacts**. *Epidemiol Infect* 2005, **133**:1119-1122.

47. Lipsitch M, Cohen T, Cooper B, Robins JM, Ma S, James L, Gopalakrishna G, Chew SK, Tan CC, Samore MH *et al.*: **Transmission dynamics and control of severe acute respiratory syndrome**. *Science* 2003, **300**:1966-1970.

48. Seto WH, Tsang D, Yung RW, Ching TY, Ng TK, Ho M, Ho LM, Peiris JS: **Advisors of expert SgoHA: effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS)**. *Lancet* 2003, **361**:1519-1520.

49. 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.

50. Haagmans BL, Al Dhahiry SH, Reusken CB, Raj VS, Galiano M, Myers R, Godeke GJ, Jonges M, Farag E, Diab A *et al.*: **Middle East respiratory syndrome coronavirus in dromedary camels: an outbreak investigation**. *Lancet Infect Dis* 2014, **14**:140-145.

51. Reusken CB, Haagmans BL, Muller MA, Gutierrez C, Godeke GJ, Meyer B, Muth D, Raj VS, Smits-De Vries L, Corman VM *et al.*: **Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study**. *Lancet Infect Dis* 2013, **13**:859-866.

52. Lau SK, Li KS, Tsang AK, Lam CS, Ahmed S, Chen H, Chan KH, Woo PC, Yuen KY: **Genetic characterization of Betacoronavirus lineage C viruses in bats reveals marked sequence divergence in the spike protein of pipistrellus bat coronavirus HKU5 in Japanese pipistrelle: implications for the origin of the novel Middle East respiratory syndrome coronavirus**. *J Virol* 2013, **87**:8638-8650.

53. Al-Tawfiq JA, Memish ZA: **Middle East respiratory syndrome coronavirus: transmission and phylogenetic evolution**. *Trends Microbiol* 2014, **22**:573-579.

54. • Breban R, Riou J, Fontanet A: **Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk**. *Lancet* 2013, **382**:694-699
Critical assessment of the pandemic potential of MERS-CoV.

55. Memish ZA, Zumla AI, Al-Hakeem RF, Al-Rabeeah AA, Stephens GM: **Family cluster of Middle East respiratory syndrome coronavirus infections**. *N Engl J Med* 2013, **368**:2487-2494.

56. Who Mers-Cov Research Group: **State of knowledge and data gaps of Middle East respiratory syndrome coronavirus (MERS-CoV) in humans**. *PLoS Curr* 2013, **5**.

57. Cowling BJ, Park M, Fang VJ, Wu P, Leung GM, Wu JT: **Preliminary epidemiological assessment of MERS-CoV outbreak in South Korea, May to June 2015**. *Euro Surveill* 2015, **20**:7-13.

58. •• Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB *et al.*: **Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine**. *N Engl J Med* 2021, **384**:403-416
Randomized placebo-controlled phase 3 trial of Moderna mRNA vaccine.

59. •• Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, Kovyrshina AV, Lubenets NL, Grousova DM, Erokhova AS *et al.*: **Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia**. *Lancet* 2021, **397**:671-681
Randomized placebo-controlled phase 3 trial of Sputnik V adenovirus-based vaccine.

60. •• Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, Angus B, Baillie VL, Barnabas SL, Bhorat QE *et al.*: **Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials**. *Lancet* 2021, **397**:881-891
Randomized placebo-controlled phase 3 trial of Oxford/Astrazeneca adenovirus-based vaccine.

61. •• Walsh EE, Frenck RW Jr, Falsey AR, Kitchin N, Absalon J, Gurtman A, Lockhart S, Neuzil K, Mulligan MJ, Bailey R *et al.*: **Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates**. *N Engl J Med* 2020, **383**:2439-2450
Randomized placebo-controlled phase 3 trial of BioNTech/Pfizer mRNA vaccine.

62. Shah A, Gribben C, Bishop J, Hanlon P, Caldwell D, Wood R, Reid M, McMenamin J, Goldberg D, Srtockton D *et al.*: **Effect of vaccination on transmission of COVID-19: an observational study in healthcare workers and their households**. *medRxiv* 2021.

63. • Munoz-Fontela C, Dowling WE, Funnell SGP, Gsell PS, Riveros-Balta AX, Albrecht RA, Andersen H, Baric RS, Carroll MW, Cavaleri M *et al.*: **Animal models for COVID.-19**. *Nature* 2020, **586**:509-515
Excellent review of animal models of SARS-CoV-2.

64. Gong SR, Bao LL: **The battle against SARS and MERS coronaviruses: reservoirs and animal models**. *Anim Model Exp Med* 2018, **1**:125-133.

65. Lee P, Kim DJ: **Newly emerging human coronaviruses: animal models and vaccine research for SARS, MERS, and COVID-19**. *Immune Netw* 2020, **20**:e28.

66. Singh A, Singh RS, Sarma P, Batra G, Joshi R, Kaur H, Sharma AR, Prakash A, Medhi B: **A comprehensive review of animal models for coronaviruses: SARS-CoV-2, SARS-CoV, and MERS-CoV**. *Virol Sin* 2020, **35**:290-304.

67. Mykytyn AZ, Lamers MM, Okba NMA, Breugem TI, Schipper D, van den Doel PB, van Run P, van Amerongen G, de Waal L, Koopmans MPG *et al.*: **Susceptibility of rabbits to SARS-CoV-2**. *Emerg Microbes Infect* 2021, **10**:1-7.

68. WHO: *Consensus Document on the Epidemiology of Severe Acute Respiratory Syndrome (SARS)*. https://apps.who.int/iris/handle/10665/708632003.

69. Martina BE, Haagmans BL, Kuiken T, Fouchier RA, Rimmelzwaan GF, Van Amerongen G, Peiris JS, Lim W, Osterhaus AD: **Virology: SARS virus infection of cats and ferrets**. *Nature* 2003, **425**:915.

70. Sit THC, Brackman CJ, Ip SM, Tam KWS, Law PYT, To EMW, Yu VYT, Sims LD, Tsang DNC, Chu DKW *et al.*: **Infection of dogs with SARS-CoV-2**. *Nature* 2020, **586**:776-778.

71. Barrs VR, Peiris M, Tam KWS, Law PYT, Brackman CJ, To EMW, Yu VYT, Chu DKW, Perera R, Sit THC: **SARS-CoV-2 in quarantined domestic cats from COVID-19 households or**

close contacts, Hong Kong, China. *Emerg Infect Dis* 2020, **26**:3071-3074.

72. Neira V, Brito B, Aguero B, Berrios F, Valdes V, Gutierrez A, Ariyama N, Espinoza P, Retamal P, Holmes EC *et al.*: **A household case evidences shorter shedding of SARS-CoV-2 in naturally infected cats compared to their human owners**. *Emerg Microbes Infect* 2020:1-22.

73. Ferasin L, Fritz M, Ferasin H, Becquart P, Legros V, Leroy EM: **Myocarditis in naturally infected pets with the British variant of COVID-19**. *bioRxiv* 2021.

74. Gaudreault NN, Trujillo JD, Carossino M, Meekins DA, Morozov I, Madden DW, Indran SV, Bold D, Balaraman V, Kwon T *et al.*: **SARS-CoV-2 infection, disease and transmission in domestic cats**. *Emerg Microbes Infect* 2020, **9**:2322-2332.

75. Shi J, Wen Z, Zhong G, Yang H, Wang C, Huang B, Liu R, He X, Shuai L, Sun Z *et al.*: **Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2**. *Science* 2020, **368**:1016-1020.

76. Bosco-Lauth AM, Hartwig AE, Porter SM, Gordy PW, Nehring M, Byas AD, VandeWoude S, Ragan IK, Maison RM, Bowen RA: **Experimental infection of domestic dogs and cats with SARS-CoV-2: pathogenesis, transmission, and response to reexposure in cats**. *Proc Natl Acad Sci U S A* 2020, **117**:26382-26388.

77. Halfmann PJ, Hatta M, Chiba S, Maemura T, Fan S, Takeda M, Kinoshita N, Hattori SI, Sakai-Tagawa Y, Iwatsuki-Horimoto K *et al.*: **Transmission of SARS-CoV-2 in domestic cats**. *N Engl J Med* 2020, **383**:592-594.

78. Koopmans M: **SARS-CoV-2 and the human-animal interface: outbreaks on mink farms**. *Lancet Infect Dis* 2021, **21**:18-19.

79. Molenaar RJ, Vreman S, Hakze-van der Honing RW, Zwart R, de Rond J, Weesendorp E, Smit LAM, Koopmans M, Bouwstra R, Stegeman A *et al.*: **Clinical and pathological findings in SARS-CoV-2 disease outbreaks in farmed mink (*Neovison vison*)**. *Vet Pathol* 2020, **57**:653-657.

80. Oreshkova N, Molenaar RJ, Vreman S, Harders F, Oude Munnink BB, Hakze-van der Honing RW, Gerhards N, Tolsma P, Bouwstra R, Sikkema RS *et al.*: **SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020**. *Euro Surveill* 2020, **25**:11.

81. • Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, Molenaar RJ, Munger E, Molenkamp R, van der Spek A, Tolsma P, Rietveld A, Brouwer M *et al.*: **Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans**. *Science* 2021, **371**:172-177

This study uses whole genome sequencing to characterize chains of transmission between humans and mink and *vice versa*.

82. Boklund A, Hammer AS, Quaade ML, Rasmussen TB, Lohse L, Strandbygaard B, Jorgensen CS, Olesen AS, Hjerpe FB, Petersen HH *et al.*: **SARS-CoV-2 in Danish mink farms: course of the epidemic and a descriptive analysis of the outbreaks in 2020**. *Animals (Basel)* 2021, **11**:164.

83. Hammer AS, Quaade ML, Rasmussen TB, Fonager J, Rasmussen M, Mundbjerg K, Lohse L, Strandbygaard B, Jorgensen CS, Alfaro-Nunez A *et al.*: **SARS-CoV-2 transmission between mink (*Neovison vison*) and humans, Denmark**. *Emerg Infect Dis* 2021, **27**:547-551.

84. Larsen CS, Paludan SR: **Corona's new coat: SARS-CoV-2 in Danish minks and implications for travel medicine**. *Travel Med Infect Dis* 2020, **38**:101922.

85. Enkirch T, von Messling V: **Ferret models of viral pathogenesis**. *Virology* 2015, **479-480**:259-270.

86. Blanco-Melo D, Nilsson-Payant BE, Liu WC, Uhl S, Hoagland D, Moller R, Jordan TX, Oishi K, Panis M, Sachs D *et al.*: **Imbalanced host response to SARS-CoV-2 drives development of COVID-19**. *Cell* 2020, **181**:1036-1045 e1039.

87. Kim YI, Kim SG, Kim SM, Kim EH, Park SJ, Yu KM, Chang JH, Kim EJ, Lee S, Casel MAB *et al.*: **Infection and rapid transmission of SARS-CoV-2 in ferrets**. *Cell Host Microbe* 2020, **27**:704-709 e702.

88. Ryan KA, Bewley KR, Fotheringham SA, Slack GS, Brown P, Hall Y, Wand NI, Marriott AC, Cavell BE, Tree JA *et al.*: **Dose-dependent response to infection with SARS-CoV-2 in the ferret model and evidence of protective immunity**. *Nat Commun* 2021, **12**:81.

89. Schlottau K, Rissmann M, Graaf A, Schon J, Sehl J, Wylezich C, Hoper D, Mettenleiter TC, Balkema-Buschmann A, Harder T *et al.*: **SARS-CoV-2 in fruit bats, ferrets, pigs, and chickens: an experimental transmission study**. *Lancet Microbe* 2020, **1**:e218-e225.

90. • de Vries RD, Schmitz KS, Bovier FT, Predella C, Khao J, Noack D, Haagmans BL, Herfst S, Stearns KN, Drew-Bear J *et al.*: **Intranasal fusion inhibitory lipopeptide prevents direct-contact SARS-CoV-2 transmission in ferrets**. *Science* 2021, **371**:1379-1382

This study shows that intranasal administration of a fusion inhibitory lipopeptide can prevent direct contact transmission in ferrets.

91. Richard M, Kok A, de Meulder D, Bestebroer TM, Lamers MM, Okba NMA, Fentener van Vlissingen M, Rockx B, Haagmans BL, Koopmans MPG *et al.*: **SARS-CoV-2 is transmitted via contact and via the air between ferrets**. *Nat Commun* 2020, **11**:3496.

92. Everett HE, Lean FZX, Byrne AMP, van Diemen PM, Rhodes S, James J, Mollett B, Coward VJ, Skinner P, Warren CJ *et al.*: **Intranasal infection of ferrets with SARS-CoV-2 as a model for asymptomatic human infection**. *Viruses* 2021, **13**:113.

93. Kim YI, Yu KM, Koh JY, Kim EH, Kim SM, Kim EJ, Casel MA, Rollon R, Jang SG, Song MS *et al.*: **Age-dependent pathogenic characteristics of SARS-CoV-2 infection in ferrets**. *Res Sq* 2021 http://dx.doi.org/10.21203/rs.3.rs-131380/v2.

94. •• Kutter JS, de Meulder D, Bestebroer TM, Lexmond P, Mulders A, Richard M, Fouchier RAM, Herfst S: **SARS-CoV and SARS-CoV-2 are transmitted through the air between ferrets over more than one meter distance**. *Nat Commun* 2021, **12**:1653

This study demonstrates that SARS-CoV and SARS-CoV-2 can remain infectious when transmitted through the air over more than one-meter distance.

95. • Cox RM, Wolf JD, Plemper RK: **Therapeutically administered ribonucleoside analogue MK-4482/EIDD-2801 blocks SARS-CoV-2 transmission in ferrets**. *Nat Microbiol* 2021, **6**:11-18

This study demonstrates that treatment of SARS-CoV-2-infected ferrets with an oral drug can prevent onward transmission to susceptible animals.

96. Chan JF, Zhang AJ, Yuan S, Poon VK, Chan CC, Lee AC, Chan WM, Fan Z, Tsoi HW, Wen L *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**:2428-2446.

97. •• Sia SF, Yan LM, Chin AWH, Fung K, Choy KT, Wong AYL, Kaewpreedee P, Perera R, Poon LLM, Nicholls JM *et al.*: **Pathogenesis and transmission of SARS-CoV-2 in golden hamsters**. *Nature* 2020, **583**:834-838

Demonstration of infection, disease and transmission of SARS-CoV-2 in hamsters.

98. Imai M, Iwatsuki-Horimoto K, Hatta M, Loeber S, Halfmann PJ, Nakajima N, Watanabe T, Ujie M, Takahashi K, Ito M *et al.*: **Syrian hamsters as a small animal model for SARS-CoV-2 infection and countermeasure development**. *Proc Natl Acad Sci U S A* 2020, **117**:16587-16595.

99. Boudewijns R, Thibaut HJ, Kaptein SJF, Li R, Vergote V, Seldeslachts L, Van Weyenbergh J, De Keyzer C, Bervoets L, Sharma S *et al.*: **STAT2 signaling restricts viral dissemination but drives severe pneumonia in SARS-CoV-2 infected hamsters**. *Nat Commun* 2020, **11**:5838.

100. Osterrieder N, Bertzbach LD, Dietert K, Abdelgawad A, Vladimirova D, Kunec D, Hoffmann D, Beer M, Gruber AD, Trimpert J: **Age-dependent progression of SARS-CoV-2 infection in Syrian hamsters**. *Viruses* 2020, **12**:779.

101. Kaptein SJF, Jacobs S, Langendries L, Seldeslachts L, Ter Horst S, Liesenborghs L, Hens B, Vergote V, Heylen E, Barthelemy K *et al.*: **Favipiravir at high doses has potent antiviral activity in SARS-CoV-2-infected hamsters, whereas**

hydroxychloroquine lacks activity. *Proc Natl Acad Sci U S A* 2020, **117**:26955-26965.

102. Rogers TF, Zhao F, Huang D, Beutler N, Burns A, He WT, Limbo O, Smith C, Song G, Woehl J *et al.*: **Isolation of potent SARS-CoV-2 neutralizing antibodies and protection from disease in a small animal model**. *Science* 2020, **369**:956-963.

103. Sanchez-Felipe L, Vercruysse T, Sharma S, Ma J, Lemmens V, Van Looveren D, Arkalagud Javarappa MP, Boudewijns R, Malengier-Devlies B, Liesenborghs L *et al.*: **A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate**. *Nature* 2021, **590**:320-325.

104. Port JR, Yinda CK, Owusu IO, Holbrook M, Fischer R, Bushmaker T, Avanzato VA, Schulz JE, van Doremalen N, Clancy CS *et al.*: **SARS-CoV-2 disease severity and transmission efficiency is increased for airborne but not fomite exposure in Syrian hamsters**. *bioRxiv* 2020.

105. van Doremalen N, Purushotham J, Schulz J, Holbrook M, Bushmaker T, Carmody A, Port J, Yinda KC, Okumura A, Saturday G *et al.*: **Intranasal ChAdOx1 nCoV-19/AZD1222 vaccination reduces shedding of SARS-CoV-2 D614G in rhesus macaques**. *bioRxiv* 2021.

106. Selvaraj P, Lien CZ, Liu S, Stauft CB, Nunez IA, Hernandez M, Nimako E, Ortega MA, Starost MF, Dennis JU *et al.*: **SARS-CoV-2 infection induces protective immunity and limits transmission in Syrian hamsters**. *Life Sci Alliance* 2021, **4**:e202000886.

107. Tostanoski LH, Wegmann F, Martinot AJ, Loos C, McMahan K, Mercado NB, Yu J, Chan CN, Bondoc S, Starke CE *et al.*: **Ad26 vaccine protects against SARS-CoV-2 severe clinical disease in hamsters**. *Nat Med* 2020, **26**:1694-1700.

108. Chan JF, Yuan S, Zhang AJ, Poon VK, Chan CC, Lee AC, Fan Z, Li C, Liang R, Cao J *et al.*: **Surgical mask partition reduces the risk of noncontact transmission in a golden Syrian hamster model for coronavirus disease 2019 (COVID-19)**. *Clin Infect Dis* 2020, **71**:2139-2149.

109. Lee AC, Zhang AJ, Chan JF, Li C, Fan Z, Liu F, Chen Y, Liang R, Sridhar S, Cai JP *et al.*: **Oral SARS-CoV-2 inoculation establishes subclinical respiratory infection with virus shedding in golden Syrian hamsters**. *Cell Rep Med* 2020, **1**:100121.

110. Korber B, Fischer WM, Gnanakaran S, Yoon H, Theiler J, Abfalterer W, Hengartner N, Giorgi EE, Bhattacharya T, Foley B *et al.*: **Tracking changes in SARS-CoV-2 spike: evidence that D614G increases infectivity of the COVID-19 virus**. *Cell* 2020, **182**:812-827 e819.

111. Zhou B, Thi Nhu Thao T, Hoffmann D, Taddeo A, Ebert N, Labroussaa F, Pohlmann A, King J, Steiner S, Kelly JN *et al.*: **SARS-CoV-2 spike D614G change enhances replication and transmission**. *Nature* 2021, **592**:122-127.

112. Blair RV, Vaccari M, Doyle-Meyers LA, Roy CJ, Russell-Lodrigue K, Fahlberg M, Monjure CJ, Beddingfield B, Plante KS, Plante JA *et al.*: **Acute respiratory distress in aged, SARS-CoV-2-infected African green monkeys but not rhesus macaques**. *Am J Pathol* 2021, **191**:274-282.

113. Singh DK, Singh B, Ganatra SR, Gazi M, Cole J, Thippeshappa R, Alfson KJ, Clemmons E, Gonzalez O, Escobedo R *et al.*: **Responses to acute infection with SARS-CoV-2 in the lungs of rhesus macaques, baboons and marmosets**. *Nat Microbiol* 2021, **6**:73-86.

114. Smits SL, de Lang A, van den Brand JM, Leijten LM, van IWF, Eijkemans MJ, van Amerongen G, Kuiken T, Andeweg AC, Osterhaus AD *et al.*: **Exacerbated innate host response to SARS-CoV in aged non-human primates**. *PLoS Pathog* 2010, **6**: e1000756.

115. Bauer DC, Tay AP, Wilson LOW, Reti D, Hosking C, McAuley AJ, Pharo E, Todd S, Stevens V, Neave MJ *et al.*: **Supporting pandemic response using genomics and bioinformatics: a case study on the emergent SARS-CoV-2 outbreak**. *Transbound Emerg Dis* 2020, **67**:1453-1462.

116. McCarthy KR, Rennick LJ, Nambulli S, Robinson-McCarthy LR, Bain WG, Haidar G, Duprex WP: **Recurrent deletions in the SARS-CoV-2 spike glycoprotein drive antibody escape**. *Science* 2021, **371**:1139-1142.

117. Montagutelli X, Prtot M, Levilayer L, BS E, Jouvion G, Conquet L, Donati F, Albert M, Gamaro F, Behilil S *et al.*: **The B1.351 and P.1 variants extend SARS-CoV-2 host range to mice**. *bioRxiv* 2021.