



# Domestic animals and Covid-19

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# Game plan

- ▶ Examine recent articles on cats, dogs, and other creatures from Noah's ark, related to their susceptibility to SARS-CoV-2, and to transmission potential within and between species



# Objectives

- ▶ Recite key findings from animal SARS-CoV-2 transmission study papers
- ▶ Recognize shortcomings of the animal experiments and suggest expanded set of experiments
- ▶ Write down ways you can use the information to counsel patients and others who live with household animals or who own farm animals, and who may ask you about animal-related risk
- ▶ Pass a quiz—this one will be harder than others

# Take home messages

- ▶ Our human research would be facilitated if we had a good animal model that could mimic human response to SARS-CoV-2 viral challenge
- ▶ Both dogs and cats mount a rapid antibody response to SARS
- ▶ Both species show no (or few) clinical signs after inoculation with virus, and cats quit shedding virus quickly
- ▶ Cats with initial infection do not express virus when re-inoculated
- ▶ Cats demonstrate high viral shedding and can easily transmit to other cats via aerosol and/or droplets
- ▶ Common farm animals like poultry and pigs, do not get SARS-CoV-2 based on very limited studies to date
- ▶ The implications of cross species SARS-CoV-2 transmission are enormous

# Introduction

- ▶ Reports (rare) of transmission between humans and domestic cats and dogs
- ▶ Reports of transmission from humans to tigers and lions at Bronx Zoo
- ▶ Editorial in NEJM raised question of cats playing a role as 'silent intermediary' in human cases (touched upon by Dr. Mera some months ago; Halfmann et al)
- ▶ Ferrets used as animal models for SARS-CoV-2 transmission (Shi et al, Science 2020), and pet ferrets are surprisingly common in this country

Roles of dogs and most outdoor domesticated animals that we contact not evaluated as to susceptibility/transmission

# Intro, cntd

- ▶ Development of an animal model could help our research efforts for humans and for animals re: prevention/vaccine development
- ▶ Macaques, ferrets, hamsters develop signs of disease that do not mimic the entire spectrum as humans (mostly very mild signs)
- ▶ Cat infection may be very common in 'hot spots': Wuhan cat serosurvey indicated 14.7% of cats had antibody to SARS-CoV-2
- ▶ Mink in the Netherlands apparently acquired infection from symptomatic mink farmer/s
- ▶ So far, no clear evidence of husbandry animals or household pets transmitting Covid-19 to humans

# What makes the (common) pet cross-species transmission issue potentially disastrous for humans?

- ▶ 89,700,000 dogs in US in 2017
- ▶ 900,000,000 dogs estimated in the world in 2020
- ▶ 95,600,000 cats in US (about 1 million of them live on my block)
- ▶ 200,000,000 to 600,000,000 cats estimated in the world in 2020
- ▶ 5,000,000 to 7,000,000 pet ferrets in US (third most common companion animal....Who knew?)



# Other animals susceptible to SARS-CoV-2 infection

- ▶ Cynomolgus macaques
- ▶ Grivets
- ▶ Common marmosets
- ▶ Perhaps a variety of animals sold in Chinese wet markets...unclear

# Study design, PNAS study

- ▶ 7 cats, 3 dogs in separate experiments
- ▶ 3 cats inoculated, followed over time for viral shedding, antibody response, clinical signs of illness
- ▶ They were rechallenged later with another inoculation
- ▶ 2 additional cats inoculated and 2 companion cats put into same room for transmission studies...followed over time for viral shedding, antibody response, clinical illness (like a feline Covid party)
  
- ▶ 3 dogs inoculated, followed over time for same outcomes
- ▶ No transmission studies performed on them

# key findings from PNAS study

- ▶ Cats highly susceptible to SARS-CoV-2 infection upon inoculation
- ▶ No clinical signs in cats or dogs
- ▶ Cats excreted virus from upper airway post inoculation
- ▶ Cats capable of aerosol and/or droplet spread to nearby cats that were not prior infected
- ▶ Cats capable of robust immune response that prevented a second infection when re-challenged
- ▶ Dogs seroconverted after inoculation
- ▶ Dogs did not shed virus from upper airway following infection

# Key findings, cntd

- ▶ Necropsy findings of cats showed respiratory track inflammation and signs consistent with Covid-19, despite lack of clinical signs
- ▶ Viral shedding post inoculation in cats was short duration (5 days)
- ▶ The transmission experiment parallels the findings in the NEJM study on cats reported earlier in NEJM (covered by Dr. Mera), with more details on kinetics of viral shedding in the PNAS study

# Limitations of study/ies

- ▶ Very small numbers of animals (7 cats, 3 dogs)
- ▶ Not clear if authors were describing droplet spread vs aerosol...which many of us may consider a major distinction (in earlier cat study, cages were placed side by side, resulting in transmission)
- ▶ Cats are particularly hard to study in such settings...other investigators reported difficulty gathering all samples they wanted
- ▶ Role of aging and acquisition of SARS-CoV-2 not fully evaluated
- ▶ Cross-species transmission study in experimental settings is apparently wide open for research

# Clinical signs reported in some infected pet dogs (most reports indicate only mild signs of illness)

- ▶ Temp elevation
- ▶ Coughing
- ▶ Difficulty breathing
- ▶ Lethargy
- ▶ Discharge from eyes and/or nose
- ▶ Vomiting
- ▶ Diarrhea

# Animal models for Covid-19

- ▶ At present, we seem to be lacking an animal model that mimics the full range of human disease, from asymptomatic to cytokine storm-type reaction with multiple organ system involvement
- ▶ So, how might we choose a good animal model?

# Choosing the right animal model for inf disease research (Swearengen 2018)

Although this process begins with a one-to-one comparison of the pathological progression of the disease, conceptually the collective analysis provides a many-to-many perspective. As a model is selected and validated, analysis may focus on a one-to-one approach to modeling. The basic steps to identify and develop an animal model are as follows:

1. Define the research objective.
2. Define the intrinsic factors associated with the biological phenomenon under investigation, such as the pathological progression of the disease process.
3. Define the extrinsic factors associated with the biological phenomenon under investigation such as the method used to prepare the pathogenic bacteria.
4. Create a search strategy and review the literature of previous animal models.
5. Create a biological information matrix.
6. Define unique research resources.
7. Identify preliminary animal models of choice.
8. Conduct research to fill critical gaps of knowledge in the biological information matrix for the preliminary animal models of choice.
9. Evaluate the validity of the animal models of choice.
10. Identify animal models of choice.



# Public health and other messages

- ▶ Although common household pets can get infected and mount immune responses, they are probably not very important factors in our human pandemic at present
- ▶ CDC has guidelines about Covid-19 and pets (cautious advice to pet owners, particularly if someone in household has Covid); see One Health and other CDC sites
- ▶ There is a lot more to learn about common animals in our lives, and Covid transmission risk (in both directions)
- ▶ Earlier viral transmission patterns among wild animals (ex: rabies) with cross species transmission and movement of rhabdoviruses across the country 'sound an alarm' (no evidence of that with SARS-CoV-2 at present)

# Guidance and recommendations

- [Interim Guidance for Public Health Professionals Managing People with COVID-19 in Home Care and Isolation Who Have Pets or Other Animals](#)
- Interim recommendations for intake of companion animals from households where humans with COVID-19 are present [!\[\]\(467d80e979964f7f8c752fb22248b5b7\_img.jpg\)](#)
- [Interim Infection Prevention and Control Guidance for Veterinary Clinics](#)
- [Evaluation for SARS-CoV-2 Testing in Animals](#)
- [Interim Guidance for SARS-CoV-2 Testing in North American Wildlife](#)
- [Toolkit: One Health Approach to Address Companion Animals with SARS-CoV-2](#)
- [COVID-19 Recommendations for Pet Stores, Pet Distributors, and Pet Breeding Facilities](#)

# One Health at CDC

One Health is a collaborative, multisectoral, and transdisciplinary approach — working at the local, regional, national, and global levels — with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

# One Health, cntd

One Health is an approach that recognizes that the health of people is closely connected to the health of animals and our shared environment. One Health is not new, but it has become more important in recent years. This is because many factors have changed interactions between people, animals, plants, and our environment.

- Human populations are growing and expanding into new geographic areas. As a result, more people live in close contact with wild and domestic animals, both livestock and pets. Animals play an important role in our lives, whether for food, fiber, livelihoods, travel, sport, education, or companionship. Close contact with animals and their environments provides more opportunities for diseases to pass between animals and people.
- The earth has experienced changes in climate and land use, such as deforestation and intensive farming practices. Disruptions in environmental conditions and habitats can provide new opportunities for diseases to pass to animals.
- The movement of people, animals, and animal products has increased from international travel and trade. As a result, diseases can spread quickly across borders and around the globe.

## ONE HEALTH Fact Sheet



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# Three relevant concerns related to One Health perspective (Hernandez et al)

- ▶ Livestock infection and transmission from handling or from eating poultry or other meat: no documented events
- ▶ Companion animals and their viral S protein sequences look almost identical to human S protein viral isolates (Hernandez et al)
- ▶ Wet markets and handling and eating bush animals remain potentially problematic, although China has implemented some restrictions based on an international news report recently

# Time for a quiz. You may need a pencil or pen. Or fancy tablet.

- ▶ Name 5 species of animals that can become infected with SARS-CoV-2, either naturally or via experimental inoculation
- ▶ Among experimentally-infected cats in the PNAS study, was viral shedding A) short in duration (less than a week), or B) longer duration, more than a week?
- ▶ What is One Health and why is their mission relevant to the current pandemic?
- ▶ Draw a picture of a grivet (email your drawings to David or Eric later, no googling grivets ahead of time)

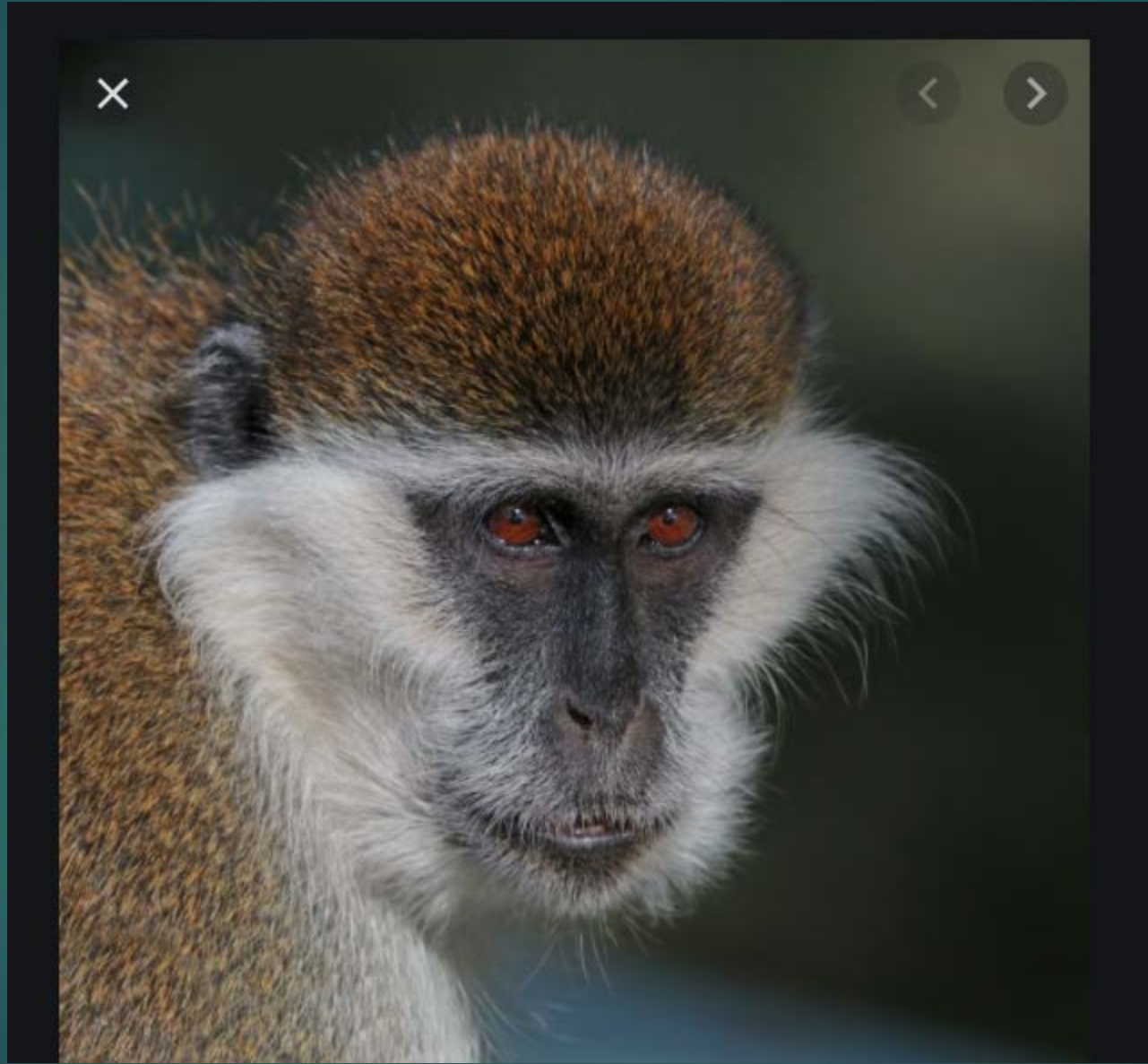
What happens if you bring a Covid-19 canine into a pediatric-age group birthday party? A) nothing B) 50% or more of the participants will develop Covid-19) C) too early to tell, the party was just last Friday



# References

- ▶ Hernandez et al, Pathogens 2020 9(6)
- ▶ Swearengen JR. Choosing the right animal model. Animal Models and Experimental Medicine. July 2018  
<https://doi.org/10.1002/ame2.12020>
- ▶ Bosco-Lauth et al. Experimental infection of dogs and cats with SARS-CoV-2. PNAS 2020
- ▶ Halfmann et al. Transmission of SARS-CoV-2 in domestic cats. NEJM 2020 editorial
- ▶ Grazia: 'Non ho trovato I rapporti sta settimana..Tomasso ha fatto tutto. Adesso, vorrei andare con il mio griveto.'









**Figure 1.** Phylogenetic analysis of amino acid sequences of the angiotensin-converting enzyme 2 (ACE2) receptor in different animals and humans. The ACE2 orthologous amino acid sequences were downloaded from NCBI (<https://www.ncbi.nlm.nih.gov/gene/59272/ortholog/?scope=33554>) and aligned with COBALT ([https://www.ncbi.nlm.nih.gov/tools/cobalt/re\\_cobalt.cgi](https://www.ncbi.nlm.nih.gov/tools/cobalt/re_cobalt.cgi)). The tree was generated using a maximum likelihood estimate with FastTree, under a JTT model. The graphic representation was made with the ggtree package in R, and each color in the multiple sequence alignment (msa) corresponds to an amino acid.

