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NEWSLETTER

The COVID-19 Pandemic Continues- and is Worse!

Evelyn E. Zuckerman, Editor **Winter 2021** **Vol. 20, Number 1**

In This Issue:

Inauguration day, January 20, 2021, was the 1-year anniversary of the first case of COVID-19 diagnosed in this country, and after 27 million infections with SARS-CoV-2 and 468,217 deaths, and the slow roll-out of the vaccine, I am struggling to understand how such an "advanced" country has allowed this to happen. Some milestones from this year: 93,000 deaths worldwide just in the last week, and a record 4,375 Americans died of COVID on inauguration day. This issue of the Newsletter will discuss some current aspects of the world-wide continuing, and worsening, pandemic in people and animals.

Dr. Anthony Palminteri:

Another friend, and major influence in my veterinary career, Dr. Tony Palminteri, a co-owner of the Oradell Animal Hospital (OAH) in Paramus, NJ died on November 10, 2020 (non-COVID-19 related). He was the first board certified veterinary surgeon in New Jersey, and the OAH was the first veterinary referral hospital in New Jersey. Tony was able to discuss veterinary hospital architectural best practices as easily as he answered orthopedic surgery questions. He was always active, he achieved the 9th Dan rank in Ju Jitsu, loved to sail, ski, and garden.

Dr. Tony Palminteri at the dedication, in 2002, of the new Oradell Animal Hospital, which he designed.

Tony allowed me to investigate cases of FeLV infected cats, in the early 1970s, at OAH, which enabled us to discover the contagious transmission and clinical spectrum of the virus. We performed most of our epidemiological and clinical studies of *Bartonella* from pet cats at the hospital in the 1990s. He even hired me for moonlight work at the hospital when I first began my research career in 1967. Our families have been good friends for 54 years. Tony will be greatly missed by family, friends, veterinary medicine and, by me.
Bill Hardy

Why is the Pandemic Worse?

The pandemic is worse due to holiday gatherings, lack of routine mask wearing in many parts of the country, pandemic fatigue, and politics. As of the printing of this Newsletter, **February 10, 2021**, the data are staggering: **world-wide infections 107,011,739 and deaths 2,343,666, USA infections 27,193,849 and deaths 468,217 (Johns Hopkins Univ Med, http://coronvirus.jhu.edu/)**. Our only hope to control this virus is through effective worldwide vaccine implementation, development of an effective therapy and a worldwide political will for implementation of remediation programs.

Animals:

We continue to review the animal SARS-CoV-2 world literature to find what animals are susceptible to this virus.[1] It is imperative to determine if any pet, or peridomestic, wild, or endangered animals can become a natural reservoir for this virus and possibly transmit the virus back to susceptible people. The list of animals susceptible to infection with the SARS-CoV-2 virus is increasing as indicated in the following tables. The virus has been confirmed in 3 families of the Order Carnivora: canids- dogs and racoons, felids- pet cats, tigers, lions, pumas/cougars and snow leopards, and mustelids- minks and ferrets. These findings are alarming in that new animal species, replicating the SARS-CoV-2, may create an uncontrollable reservoir that may create even more pathogenic viral variants which may be capable of jumping back to humans or to other species.

Pet cats can be infected from their owners and can transmit the virus to other cats by the aerosol route. To date, no pet cats have been shown to be able to transmit the virus back to people, but minks are able to do so (see the USDA data, as of January 15, 2021, on the back of the Newsletter). Pet dogs and cats are the species most often exposed to infected people, whereas mink breeding facilities worldwide, have the most infected animals due to their crowded housing facilities.

Now the question is: should a vaccine be developed for pets and other animals? There is a pet cat SARS-CoV-2 vaccine in development. Do we need a vaccine for endangered non-human primates and other endangered species? Translating the human vaccine methods to animal species should be relatively easy.

In Africa, the COVID-19 pandemic creates a wildlife crisis by reduced funding due to tourist reductions, restrictions on the operations of conservation agencies and wildlife managers, and increased human threats to wildlife.[2]

SARS-CoV-2 Susceptibility of Peridomestic Wildlife Animals

Animal	Susceptible & Shed Virus
Deer mice	Yes
Bushy-tailed wood rats	Yes
Striped skunks	Yes
Mink	Yes & Shed
Ferrets	Yes & Shed
Fruit bats	Yes & Shed
White-tailed deer	Yes
Racoons	Yes
House mice	No
Cottontail rabbits	No
Black-tailed prairie dogs	No
Fox Squirrels	No

SARS-CoV-2 Susceptibility of Pet Animals

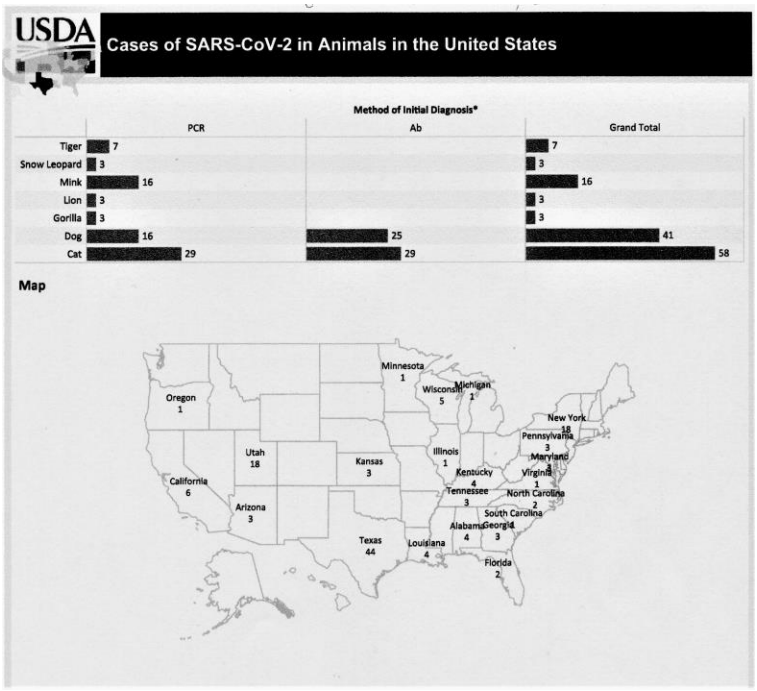
Animal	Susceptible & Shed Virus
Cats	Yes & Shed
Dogs	Yes
Ferrets	Yes & Shed
Hamsters	Yes

SARS-CoV-2 Susceptibility of Farm Animals

Animal	Susceptible & Shed Virus
Cattle	No
Pigs	No
Horses	No
Chickens	No
Ducks	No

SARS-CoV-2 Susceptibility of Wild Animals

Animal	Susceptible & Shed Virus
Lions (zoo)	Yes
Tigers (zoo)	Yes
Gorillas (zoo)	Yes
Snow leopards (Zoo)	Yes
Pumas/cougars	Yes
Grivets	Yes
Tree shrews	Yes
Rhesus monkeys	Yes
Cynomolgus macaques	Yes
Common marmosets	Yes
Pangolins	Yes



National Veterinary Services Laboratory data: Updated January 15, 2021.
https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.pdf
More information on COVID-19 can be found at
https://www.cdc.gov/coronavirus/2019-ncov/animals/pets-other-animals.html

SARS-CoV-2 Vaccine Platforms:

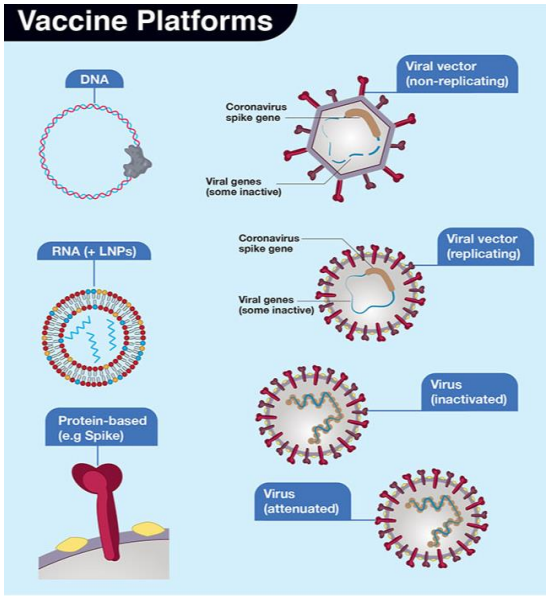


Figure 1
Credit: Colin D. Funk, Craig Laferrière, and Ali Ardakani - Funk CD, Laferrière C and Ardakani A (2020) A Snapshot of the Global Race for Vaccines Targeting SARS-CoV-2 and the COVID-19 Pandemic. Front. Pharmacol. 11:937.https://doi.org/10.3389/fphar.2020.00937, CC BY 4.0, https://commons.wikimedia.org/w/index.php?curid=99473787

There are 7 SARS-CoV-2 vaccine platforms (Figure 1). The vaccine target is the spike viral surface protein that is used by the virus to attach to susceptible cells that carry the angiotensin converting enzyme 2 (ACE-2) receptor protein. The Pfizer-BioTech COVID-19 and Moderna COVID-19 vaccines are mRNA (nucleoside-modified mRNA encoding the pre-fusion stabilized spike glycoprotein (S) of the SARS-CoV-2 virus) encased in a lipid nanoparticle to protect the fragile mRNA from degradation. This lipid nanoparticle was the breakthrough discovery that is enabling mRNA vaccinology.[3]

There are presently 2 FDA approved vaccines available and many more to come. Both are COVID-19 mRNA vaccines are given in the upper arm muscle. The mRNA instructions for the viral spike protein, within the lipid nanoparticles, are phagocytosed by muscle and dendritic immune cells. The cells then use the viral mRNA instructions to make the surface proteins of the virus. The introduced mRNA never enters the DNA in the nucleus of the cells. After the viral surface proteins are made, the cells break down releasing the SARS-CoV-2 immunogenic spike proteins and degrades the mRNA. Non-immune muscle cells can potentially absorb vaccine mRNA, manufacture spikes, and display spikes on their surfaces, however, dendritic cells absorb the mRNA nanoparticles much more avidly.

Once the dendritic cells are activated, they migrate to lymph nodes, where the antigen is presented to T and B lymphocytes which then leads to the production of antibodies and immune killer T-cells that are specifically targeted to the SARS-CoV-2 surface spike protein, resulting in immunity.

The benefit of using an mRNA vaccine is to have the vaccinee's host cells produce the antigens, under the instructions of the mRNA, which is far easier than producing the antigen proteins or attenuated viruses in bulk *ex vivo*. Speed of design and production is another advantage. Moderna designed their mRNA-1273 vaccine for COVID-19 in just 4 days after receiving the sequence of the SARS-CoV-2 virus. Another important advantage of mRNA-vaccines is that, since the immunogens are produced inside cells, they stimulate both cellular and humoral immunity.

To reiterate, mRNA vaccines do not enter into or reprogram DNA inside of vaccinee's cells. The synthetic mRNA fragment is a copy of a specific part of the viral RNA, the protein spike, and is not related to any human DNA. This misconception was circulated as the COVID-19 mRNA vaccines came to public prominence, and is a debunked conspiracy theory.

SARS-CoV-2 Viral Variants:

Currently, four new mutant variants of the SARS-CoV-2 virus have occurred that cause coronavirus disease (COVID-19). These variants seem to spread more easily and have now been found in the U.S. and many other countries.
U.K., B.1.1.7: This variant was first identified in the U.K and has 23 mutations. Several of these mutations are in the spike S protein that the virus uses to attach itself to the surface of human cells. This variant might be associated with an increased risk of death compared to other variants and has the potential to infect an estimated 50 percent more people.
South Africa, B.1.351: A variant identified in South Africa, has multiple mutations in the S protein. There's no evidence that this variant causes more severe COVID-19 disease.
Brazil, P.1: The P.1 variant has 17 mutations, including 3 in the S protein. Some evidence suggests that this variant might be less vulnerable to antibodies generated by a previous COVID-19 infection or a current vaccine.
California, L452R: This variant was identified in several large outbreaks in Santa Clara County, California. The variant carries 3 spike protein mutations.

Studies of the Pfizer-BioNTech and Moderna COVID-19 vaccines are needed to provide evidence of protection against the four variants presently identified. Vaccine manufacturers are already looking into creating booster shots to improve protection against variants. And, as with influenza viruses, SARS-CoV-2 viral variants may mean that yearly vaccinations with current prevalent strains may be needed.

SARS-CoV-2 and COVID-19 Therapy:

There has not been much progress in development of effective, life-saving therapy for SARS-CoV-2 infection or for the COVID-19 disease. We need an effective anti-viral drug. Harvard Medical School recommendations below:
Convalescent Plasma: patients who received convalescent plasma within three days of developing symptoms were 48% less likely to develop severe COVID-19 illness compared to patients who received placebos.
Monoclonal Antibody to the Surface Spike Proteins: These therapies must be given intravenously soon after developing symptoms. The treatment can reduce the risk of hospitalization and emergency room visits.
Remdesivir: Clinical trials suggest that remdesivir may modestly speed up recovery time.
Hydroxychloroquine : A paper in JAMA, reported no clinical benefits.
Dexamethasone: Patients who require supplemental oxygen or ventilators, and receive dexamethasone, are less likely to die within 28 days than those who received standard care. No benefit occurred in patients who did not need respiratory support. https://www.health.harvard.edu/diseases-and-conditions/treatments-for-covid-19

References:

1. National Veterinary Services Laboratory data: Updated January 15, 2021. https://www.aphis.usda.gov/animal_health/one_health/downloads/sars-cov2-in-animals.
2. Lindsey, P., Allan, J., Brehony, P. et al. Conserving Africa's wildlife and wildlands through the COVID-19 crisis and beyond. Nat Ecol Evol 4, 1300–1310 (2020). https://doi.org/10.1038/s41559-020-1275-6.
3. Dolgin, E. How COVID unlocked the power of RNA. Nature 589: 189-191, 2021.

SARS-CoV-2 & COVID-19 references can be obtained at: www.nlm.nih.gov