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NEWSLETTER

Similarities Between the COVID-19 and AIDS Pandemics[©]

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In This Issue: *Byline Dr. WD Hardy Jr.*

This will be our 7th NVL Newsletter concerning the COVID-19 pandemic covering 21 months. On October 9th, at 1:30 am, I was still trying to develop a topic, when I perused through the September 30th issue of the New England Journal of Medicine and found an article marking the 40th anniversary of the AIDS pandemic which was June 5, 2021.¹ After reading this article, I realize that, as a young veterinarian in research on retroviruses at Memorial Sloan-Kettering Cancer Center, I was right there at the beginning of the AIDS pandemic. This brought back memories about my own experiences and made me realize how similar both of these pandemics are. Early on in each pandemic, I lost a veterinary colleague to AIDS and 2 high school friends to COVID-19. Misinformation, political differences, indifference and prejudices, highlight(ed) both.

COVID-19 Pandemic:

The first case of COVID-19 in the United States was reported in January 21, 2020, 626 days ago. Since then, there have been 44.3 million US cases and 712,993 deaths which surpasses the 698,222 American deaths in all foreign wars from 1775 to 2020 (excluding the civil war which was fought only by Americans against Americans). <https://www.census.gov/history/pdf/wwi-casualties112018.pdf>

We have been writing about the COVID-19 pandemic, caused by SARS-CoV-2, for the past year-and-three quarters and it is still with us.

Exactly one year ago the world statistics were:

2020 Worldometer for the Pandemic

October 10th 2020: **Worldwide data***

Total infections: 37,459,161

Total deaths: 1,077,458

New infections today: 360,006

October 10th 2020: **United States data***

Total infections: 7,768,629

Total deaths: 214,844

Now, a year later the statistics are horrendous:

2021 Worldometer for the Pandemic

October 10th 2021: **Worldwide data***

Total infections: 237,719,281

Total deaths: 4,850,162

New infections today: 354,613

October 10th 2021: **United States data***

Total infections: 45,276,564

Total deaths: 734,310

New infections today: 34,966

*ProMED is an email program of the Society for Infectious Diseases

<http://www.promedmail.org>

<https://www.worldometers.info/coronavirus/#countries>

GOOD NEWS:

After this summer's COVID-19 case spike in hospitalizations and deaths that occurred in more than 90% of unvaccinated people, there is good news here- increase in vaccinations, 10% decrease in new cases and 1.7% decrease in new deaths in the USA.

Antiviral Therapy- Good News COVID-19 Therapy:

There now appears to be curative antiviral therapy for the infection.

Antiviral Therapy:

Remdesivir- (GS-5734) nucleotide analogue given by infusion. Effectiveness is disputed.

Monoclonal antibody cocktail anti-S protein by infusion- very effective.

Molnupiravir- induces RNA mutations by the viral RNA-dependent RNA polymerase (RdRp) by oral pill: 4 pills BID- 50% effective. **POSSIBLE BREAKTHROUGH**

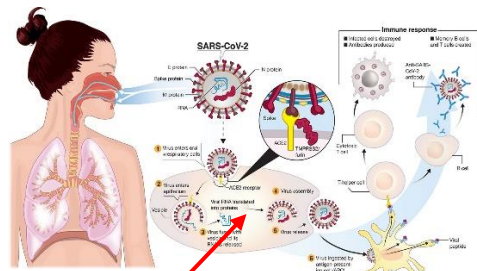
Disease Palliative Therapy:

Steroids- to dampen the cytokine storm

Antibiotics- prevent bacterial pneumonia

Immunostimulant- BCG TB vaccine

Coronaviruses use an RNA-dependent RNA polymerase (RdRp) for replication and transcription of their RNA genomes. RdRp is an obvious target for antiviral drugs. Antiviral drugs will target the viral polymerases and function as nucleoside analogues to terminate the RNA synthesis. Coronaviruses possess a proofreading activity that can remove incorrect nucleotides inserted in their RNA. Remdesivir can circumvent this proofreading and has some antiviral activity.



Colin D. Funk, Craig Laferrière, and Ali Andakani. CC BY 4.0 - <https://creativecommons.org/licenses/by/4.0/>, via Wikimedia Commons

Red Arrow: Molnupiravir inserts its NHC triphosphate, rather than the normal RNA substrate, which is incorporated causing RNA mutations and the inability to replicate.² Merck just announced their results of a study for their drug molnupiravir which interferes with the SARS-CoV-2 and inhibits replication in human lung tissue,³ blocks the virus transmission in ferrets⁴, and reduces the viral RNA in patients.⁵

The drug basically inserts so many errors into the viral RNA that it can no longer replicate. On October 1, 2021 Merck, and partner Ridgeback Biotherapeutics, filed for emergency U.S. clearance for an oral drug known as molnupiravir, which dramatically reduced the risk of hospitalizations and deaths in a Phase 3 trial. A 5-day course of therapy reduced the chances that newly diagnosed patients would be hospitalized or die by 50%. They studied 775 adults with mild-to-moderate COVID-19, who were considered higher risk for severe disease due to obesity, diabetes or heart disease. Among patients taking molnupiravir, 7.3% were either hospitalized or died at the end of 30 days, compared with 14.1% of those getting the placebo. No deaths occurred in the drug group after that time period compared with eight deaths in the placebo group. The study was stopped short due to the very favorable results.⁶

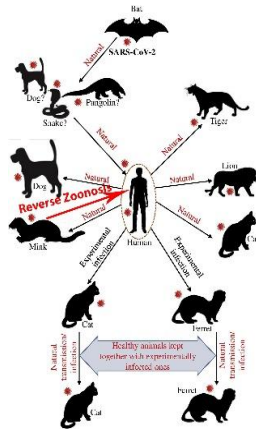
Vaccine Mandates:

Despite the Texas governor forbidding vaccine mandates, due to vaccine mandates elsewhere, Americans are getting their initial COVID-19 vaccinations at a higher rate, according to the CDC.⁷ The moving average showed 235,061 Americans started new COVID-19 vaccinations on September 25th. That average climbed for six consecutive days to peak at 252,223 on September 30th. As of October, more than 217 million (65.3%) Americans are fully vaccinated, including 76.4% ≥12 years of age, 78.2% ≥18 years of age, and 95% ≥65 years of age.

Animals Update:

Coronaviruses have been long recognized as causing pathological conditions in veterinary medicine. They infect a range of animals such as bats, wild and domestic cats, dogs, primates (gorillas), pigs, cattle, horses, camels, rodents, birds, beluga whales, beaver, seals, and other wildlife. Most animal coronaviruses infect the intestinal tract and are transmitted by the fecal-oral route. Animals are important in the COVID-19 pandemic story as the virus originated in an as yet to be discovered animal source in nature. Most evidence points to a bat coronavirus infecting an intermediate host which then infected a person in China.

A growing number of animals appear to be susceptible to the SARS-CoV-2 virus and thus may act as a new expanded reservoir for zoonotic transmission.⁸ Most alarmingly are cats and dogs who share the environment of hundreds of millions of people around the world and endangered species such as tigers, gorillas and pangolins. Even though there is no evidence to date for these species of reverse zoonosis transmission (anthropozoonotic), it certainly seems reasonable to conclude that it is possible.



Origin, Host Range & Reverse Zoonosis of SARS-CoV-2

<https://doi.org/10.1016/j.jmii.2020.06.006>

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The figure above illustrates the origin and susceptible species to SARS-CoV-2 and the example (red arrow) of reverse zoonosis (anthropozoonosis) from zoonotically-infected mink to humans in the Netherlands.⁸⁻¹⁰ This is frightening in that it illustrates that any susceptible animal may become an additional animal reservoir and source for continuation of this pandemic or through viral mutations within the mink, or other animals, to create viruses with different pathogenic properties.

Wildlife:

The Wildlife Health Specialist Group of the International Union for Conservation of Nature and the World Animal Health Organization have recently released guidelines to minimize the risk of SARS-CoV-2 transmission from people to free-ranging wild mammals.¹¹ Free-ranging wild mammals may also be susceptible to SARS-CoV-2 which may result in some becoming a reservoir of the virus which may kill susceptible endangered-species.

On June 3rd, India's first wild animal death due to coronavirus occurred in Arignar Anna Zoological Park. A 9-year-old Asiatic lioness died from the



virus. So far, ten other lions at the zoo, have also tested positive for SARS-CoV-2. As a result of this string of COVID-19 outbreaks in zoos across India, the Indian government has ordered the temporary closure of all tiger preserves to visitors.

Tourists and tiger. Bandhavgarh Tiger Preserve, Madhya Pradesh, India. Home to ~50 tigers. Photo credit, WD Hardy, Jr.

Animals and COVID-19: Deer:

Epidemiological studies of North American White-Tailed Deer show they are susceptible to SARS-CoV-2.^{12,13} The Chandler study, as yet to be reviewed, was serosurveillance of white-tailed deer from 4 U.S. states.¹³ Antibodies were detected in 152 deer (40%) by a surrogate virus neutralization test.⁹ This is a surprisingly high seroprevalence demonstrating

exposure of these deer living in close proximity to people. This pool of infected deer might act as a reservoir for spread to other wild animals, might act as a fertile area for development of more dangerous viral variants, and may act as a source for reinfection of people. The authors suggest surveying other wild animals, especially deer predators. An alert veterinarian called us to ask if deer hunters, dressing their deer kills, might be at risk from the virus. An excellent but unanswered question. The USDA recommends practicing good hygiene when processing animals and we would recommend wearing gloves and an N95 mask as well.

AIDS Pandemic Similarities:

After reading the September 30th issue of the New England Journal of Medicine article marking the 40th anniversary of the AIDS epidemic which was June 5, 2021, I realized there are many similarities between the AIDS and COVID-19 pandemics¹

2020 Worldometer AIDS Pandemic

September 18th 2021: Worldwide data

Total infections: 79,300,000

Total deaths: 36,300,000

January 1st 2020: United States data

Total infections: 1,200,000

Total deaths: 700,000

It took about 40 years for the AIDS pandemic in the US to kill as many people as the COVID-19 pandemic killed in 1.75 years.

In the beginning of the AIDS pandemic, physicians and their patients, had to endure the burden of stigma and homophobia at a moment when the government had all but turned its back on AIDS, costing precious time and lives. There are many similarities between the COVID-19 and AIDS pandemics: misinformation, political differences, indifference and prejudices, highlight(ed) both. After the sexual revolution, AIDS changed the world. HIV-1, the AIDS virus, is transmitted via exchange of bodily fluids (semen and blood), very different from SARS-CoV-2 which is mainly transmitted by respiratory droplets which makes it much more transmissible.

AIDS initially was thought, by some politicians and clergy, to be the wrath of God bestowed on gays. Some refused to treat and there were debates about whether there was a moral duty to take the risks of caring for patients with AIDS. However, when the virus got into the heterosexual population, via the blood supply, the politicians took the pandemic seriously and funds began to be forthcoming.

An emergency treatment-investigation policy was applied almost immediately in the fight against AIDS. Soon after the AIDS pandemic began and the causative agent, the HIV-1 retrovirus was discovered, the NIH began asking drug companies and researchers, with virus-killing expertise, to screen any compound for testing in secure virus labs. A biochemist at Burroughs Wellcome Company (today GlaxoSmithKline) sent a drug called zidovudine (AZT) to screen against animal retroviruses, to scientists at the National Cancer Institute, to the late Dani Bolognesi at Duke University for tests of the mouse leukemia virus and Dani also asked Evelyn Zuckerman and me, in our Laboratory of Veterinary Oncology at Memorial Sloan Kettering Institute, to screen the

compounds against our feline leukemia virus isolate. Our labs were given three dozen compounds, designated only by letters, and each lab found only the one compound, AZT, to be very active in killing our retroviruses. In mouse and feline retrovirus tests, the drug looked promising and thus a clinical human trial of AZT was launched. The trial had to be halted early when the placebo's dead-patient ratio reached 19 to 1 against AZT. Doctors can't ethically continue studies when it is clear that a drug is so effective. The FDA immediately authorized a treatment protocol for broader use of AZT. More than 4,000 AIDS patients were treated with AZT **before the FDA finalized its approval** as the first AIDS drug, now sold under the brand name Retrovir, in 1987. This protocol was exactly what was followed when the excellent COVID-19 vaccines were **authorized under emergency approval by the FDA**. The discovery of highly active antiretroviral therapy (HAART) makes HIV-1 infection treatable and AIDS a manageable, though not curable, disease like insulin is for diabetes. HAART can reduce the HIV viral load in the blood to an undetectable level and prevent the transmission of HIV via sex. We will be at that same stage with COVID-19 **IF** we can reach the proper herd immunity through vaccination.

Editorial:

It seems that we have not learned much between these 2 major and ongoing pandemics. We must review our mistakes and try to correct them before the next, inevitable, pandemic appears.

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can be obtained at:

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