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NEWSLETTER

One Health: Old and New Science for Veterinarians[®]

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In This Issue:

The Fall 2024 issue of the NVL Newsletter ends the 23rd year of our Newsletters (93 issues in total). This issue will be a potpourri of One Health issues: **two old subjects**- 1) COVID-19 and 2) A/H5N1 bird flu, and **two new subjects**- 1) a retrovirus HIV landmark Lenacapavir prevention therapy and 2) a possible link between pathogens and Alzheimer's Disease. We will try to weave a logical comparative narrative between these seemingly unrelated topics and our lab's work during the past 52 years with FeLV, FIV and *Bartonella species*.

The Old

1) COVID-19:

We have suffered greatly as a country with the COVID-19 pandemic. In battling the severe zoonotic pathogen our economy has suffered, school children have lost precious classroom time, and our population has been divided by the methods used to battle the SARS-CoV-2 virus.

Personally, I (Dr. Hardy) have been affected greatly by the pandemic. Several of my family developed COVID-19 and an extended bout of long COVID. Fortunately, all survived and now are well. However, I lost a dear high school buddy to COVID. He and I were on the opposite spectrum politically, but we loved to argue politics in a friendly fashion and after each encounter, laugh and have fun going to dinners with our families. He never ever got a flu vaccine; I would plead with him to do so but to no avail. The WHO declared COVID-19 a pandemic on March 11, 2020. In the early stages of the pandemic, he resisted the cautions recommended and listened to those who said COVID was nothing but a bad cold and masks were not needed.

As a high school wrestler, he was a champion and was the same in college. When the 2020 NCAA collegiate wrestling championships were held in a midwestern state he went. Even though he was a very healthy strong individual when he left, only a few days after returning home, he fell severely ill with COVID-19. He was hospitalized when there were no therapies available and little knowledge. From the day he entered the hospital until his death, 3 weeks later, he and his wife were unable to be in the same room together or

able to touch each other. He died on April 4, 2020, only 25 days after the pandemic was declared, and no formal funeral was possible. I still miss those wonderful arguments we had together! From that awful day, our country went on to lose more than a million more people, even though we have one of the best medical capabilities in the world.

A Divided Nation:

An excellent recent article by David Wallace-Wells, in the New York Times Opinion Section, Sunday August 11, 2024, entitled: **"Bird Flu Shows That the U.S Learned All the Wrong Lessons From Covid."** He opines that we were weary of COVID-restrictions and our divided nation turned the wrong way. Even though the pandemic is NOT over, the tracking and statistics are. There are no current data as to new cases and deaths in the USA. The government decided enough is enough and chose to weaken our public health structure by lowering funding and easing or preventing mandates for preventive measures. This is due to our divided government. Many states are now placing restrictions on even mask-wearing and preventing public health agencies from mandating mask-wearing, **even in the face of any possible new deadly pandemic.** What has happened to protecting our country? There is even a movement in congress to defund the CDC by 22%! How will our politicians come to our aid with no public health knowledge?

More than half of the states have enacted laws that hinder public health officials from doing their jobs. The excellent CDC USA wastewater pathogen testing program, which detects pathogen activity, including SARS-CoV-2 virus, in wastewater from 41 states, even before illnesses occur, is being abruptly shut down due to political pressure.¹ The most recent wastewater surveillance data from 8-9-2024 are as follows: very high SARS-CoV-2 activity in the following states: WA, OR, CA, TX, LA, FL SC, NC, ME, ID, AL, KS, AK, DC, UT, CO, MN. **We are basically flying blind now with regards to SARS-CoV-2 transmission.**

Have we forgotten that there are Americans who are immunosuppressed that need the protection of a strong independent public health apparatus? What if our next pandemic comes from a pathogen that causes more mortality in young people than the COVID-19 pandemic which was more lethal for people older than 50 years of age.

We may be looking down that barrel right now at such an upcoming pandemic with the highly pathogenic H5N1 avian flu (HPAF) in our sights.

2) Bird flu:

As Yogi Berra once said "Déjà vu all over again." Have we not learned lessons from our national nightmare with COVID-19 pandemic?² As David Wallace-Well's opinion piece ably summarizes, we are not ready for our next pandemic, and I hope Yogi is wrong.

Five Pandemics Since 1918

Year	Pandemic	Deaths	% of World Pop
1918	Spanish Flu*+	~50 million	2.68%
1957	Asian Flu*	~1.5 million	0.05%
1968	Hong Kong Flu*	1 million	1.03%
2009	Pandemic Flu*	300,000	0.004%
2019	COVID-19**	6.6 million	0.08%

* Influenza A virus

** Coronavirus SARS-CoV-2- the second most deadly and first Coronavirus pandemic.³

+ I lost my aunt (as an infant) in the 1918 flu pandemic.

The Next Zoonotic Pandemic May Already be Here- Avian Flu H5N1:

Influenza pandemics Except for smallpox, most pandemics are caused by newly evolved viruses. Influenza pandemics have occurred worldwide for centuries and are related to farming birds and pigs. The Spanish flu, also known as the 1918 influenza, was an unusually deadly influenza pandemic caused by the H1N1 influenza A virus. It lasted from February 1918 to April 1920, and infected 500 million people, about a third of the world's population at the time. The death toll is estimated to have been between 20 million and 50 million people, 2-3% of the world's population at that time.³

The World Organization for Animal Health (WOAH) has recorded more than 42 million individual cases of avian influenza in domestic and wild birds since the outbreak began in October 2021. More than 58 million domestic birds, including poultry, have died from the disease, and more than 193 million more have been culled.⁴



Chicken Farm



Migrating birds dead from bird flu

Presently, avian influenza A/H5N1 has decimated chicken flocks worldwide causing the culling of millions of birds. It has spread to numerous wild bird species and now even to some mammals. The receptors of the upper airways of birds are less common to those in mammals. However, the virus has adapted alarmingly fast to infect new hosts including many mammals. Other non-bird species infected with H5N1 are cattle, pigs, cats, dogs, ferrets, bobcats, red foxes, skunks, raccoons, black bears, otters, seals and humans.

On a mink farm in Spain, there appears to have been mink to mink transmission of the virus, which is very unusual in mammals, and may serve to generate variants that will be more infectious for people. More than 50,000 minks were killed at this facility.^{5,6}

Recently dairy cows have been infected in many states, 157 herds in 13 states by July 18, 2024.⁷ The spread to cows has been unobserved and now there has been spread to dairy workers and even to the public through raw milk. In fact, the disclosure of the transmission through unpasteurized raw milk led to a quick increased demand for unpasteurized milk!



Farmworker in a milking dairy barn

A/H5N1 Transmission:

Bird to bird transmission occurs through direct contact, through feces, and via fomites. Many of the non-bird species probably were infected by scavenging on the carcasses of H5N1-infected wild birds. Farmworkers are infected by contact with milk and by droplets. Until recently, few dairy cows have been tested and many farmworkers have refused to be tested.⁷ These decisions have been exacerbated by the COVID-19 pandemic rebellion against public health authorities and government edicts. Now there are movements to only allow public health measures to be authorized by an act of congress! We all know how well that will work! If this new version of the H5N1 bird influenza virus mutates to a similar pathogen as the 1918 strain, this flu pandemic will make the COVID-19 pandemic seem like a vacation.

The World Health Organization (WHO) says 870 humans have been infected with avian flu over the past 20 years, and 457 have died (53%). During this current outbreak, there have been a few poultry workers infected by this virus, but fortunately just a few have died.⁸ Only the inability of H5N1 to mutate within infected people has prevented the spread of the virus person-to-person that has prevented a pandemic so far. Of course, the fear is that mutants will occur which may make it more transmissible

among people and begin a pandemic which may be much more deadly than COVID-19. By comparison, only about 1% of SARS-CoV-2 infected people worldwide have died, a much lower lethality than for former bird influenza pandemics where the death rate was much higher.

The good news is this, H5N1 present variants seem less pathogenic than earlier versions, we have effective vaccines for poultry and people and, we also have effective medications. **Now we need effective surveillance and planning to prevent another catastrophic avian influenza pandemic.**

The New

FeLV and HIV are retroviruses. After HIV was discovered we were asked to test an experimental drug, AZT, in our FeLV retrovirus culture model.⁹ We found that AZT inhibited FeLV and it was then used to treat HIV-infected people. Unfortunately it was found to be effective but was too toxic. Now, 36 years later, there has been a landmark breakthrough.¹⁰⁻¹³

1) Landmark HIV Prevention:

The anti-HIV drug Lenacapavir (Sunlenca®) was tested in a phase 3 pre-exposure prophylaxis (PrEP) double-blind, randomized, controlled trial.¹⁰⁻¹³ The drug, Lenacapavir, was injected once every 6 months into 2,134 adolescent girls and young women in South Africa and Uganda. The trial was halted after 1 year when the drug was shown to be 100% effective (no new HIV infections). Among greater than 3,000 control participants, receiving approved oral pill PrEP, there were 55 new HIV infections.

Lenacapavir is novel in that it's mechanism works by attaching to the HIV capsid containing the viral genome to prevent the replication. This may be a way to finally prevent HIV infections without the development of a long sought-after HIV vaccine. However, this may not be good for HIV vaccine developers. Gilead Sciences developed the drug which will be very expensive for routine use. Gilead said it will license generics companies, in low-income countries, to produce the drug but will not to middle and high-income countries. Gilead told Reuters that Lenacapavir (Sunlenca®) injection and tablets are expected to cost \$42,250 in the first year of therapy and \$39,000 annually thereafter.

2) Pathogens and Alzheimer's Disease:

Alzheimer's is a form of dementia affecting memory, thinking, and behavior and symptoms grow to interfere with daily behavior.¹⁴ It affects between 6-10% of people older than 65 years and nearly 33% of people older than 85 years of age. The accepted etiology is described as amyloid accumulating in brain cells forming plaques after which the tau protein forms tangles which block communication between brain nerve cells. This prevents the cells from completing their processes.

A recent Alzheimer's conference had a satellite conference where the participants were gathered

to discuss the possible infectious causes of the disease.¹⁵ A report from 2018 showed that amyloid beta aggregates in the presence of herpes simplex-virus-1 a clue that the amyloid protein represents a protective response to the infection. In 2019 a report that *Porphyromonas gingivalis*, a gum disease bacterium, was found in the brains of Alzheimer's patients. When repeatedly applied to the gums of mice it triggered Alzheimer's pathology in the brains of the mice. Numerous pathogens have been found in the brains of Alzheimer's patients including *Chlamydia pneumoniae*, *Candida albicans* and HSV-1. Some feel that repeat infections and agents that can move in and out of latency are needed. The need is to show, beyond just associations, the direct proof that pathogens cause Alzheimer's disease. Chronic zoonotic infections in people, by *Bartonella species*, may also be a candidate. Our lab provided the first *Bartonella* screening test for cats 24½ years ago.

Summary: Veterinarians are dealing with the animal components of 3 worldwide zoonoses, Bartonellosis, COVID-19, and Avian Influenza. We must stay current and effective in our One Health responsibilities.

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