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# NEWSLETTER


## Where are we now in the COVID-19 Pandemic?
## The Good and The Bad©


**Evelyn E. Zuckerman, Editor** **Spring 2022** **Vol. 21, Number 2**


## In This Issue:

The Spring 2022 issue of the NVL Newsletter, released on May 10th of each year, will discuss where we are now more than 2 years into the COVID-19 pandemic. The World Health Organization declared the 2019–20 coronavirus outbreak a Public Health Emergency of International Concern on January 30, 2020, and a pandemic on March 11, 2020, exactly 2 years and 2 months ago. The world, and our country, have stumbled during this time with some excellent solutions and many missteps along the way. In a few days, we will exceed 1 million deaths in the US from COVID-19 (**1 in ~330 Americans!**), and may be at the beginning of yet another, the 5th surge (wave) with increases in cases, hospitalizations and deaths. We will discuss **The Good** and **The Bad** aspects of this medical fight. We will cover: 1) COVID-19 Statistics, 2) Diagnostic Tests, 3) Vaccines, 4) COVID-19 Disease, 5) Therapy, 6) Animals, and 7) The Future.

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## COVID-19 Statistics:

**The Bad-** The world-wide statistics, collected by the World Health Organization (WHO) Coronavirus (COVID-19) Dashboard, are grim on May 10, 2022.[1] Over the past 6 months, far more deaths have occurred in unvaccinated people than in those vaccinated.[2,3]

## WHO Dashboard for the Pandemic[1]

**USA: COVID-19 data on May 10th past 3 years:**

| | May 10, 2020 | May 10, 2021 | May 10, 2022 |
|---|---|---|---|
| **Cases:** | **28,298** | **36,823** | **82,589** |
| **Deaths** | **1,599** | **403** | **1,897** |

**Worldwide: COVID-19 data on May 10th past 3 years:**

| | May 10, 2020 | May 10, 2021 | May 10, 2022 |
|---|---|---|---|
| **Cases:** | **91,615** | **717,311** | **556,443** |
| **Deaths** | **5,150** | **12,638** | **3,243** |

**Cumulative COVID-19 data as of May 10, 2022:**

| | Cases | Deaths | % |
|---|---|---|---|
| **Global:** | **517,058,971** | **6,250,524*** | **1.2%** |
| **USA:** | **81,831,854** | **997,318** | **1.2%** |

*WHO actually estimates that 15 million people have died of COVID-19 since the start of the pandemic.

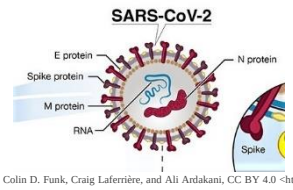
**The Good-**

**USA Fully vaccinated: 220,093,855 66.8%
USA % vaccinated by age: CDC data 5-10-2022[2]
5-11 28%, 12-17 59%, 18-48 69%, 50-64 80%, ≥65 90%

**COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)[3]

## Diagnostic Tests:

**The Good-** At home **lateral-flow antigen tests** and laboratory **PCR tests,** for detection of current infection, are available in sufficient quantities at present. These are important weapons in the fight for quick treatment that has now become available in the form of oral medications. Treatment within the first 5 days of the onset of symptoms or a positive COVID-19 test is imperative and can result in as much as 89% effective treatment to prevent severe disease and death. In addition, there are **neutralization tests** for evaluation of the strength of vaccination immunity (spike protein in figure).

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**Antigen nucleocapsid test:** A serological test for the SARS-CoV-2 **N protein** in figure above, can detect past infections, even in vaccinated people, as this test detects antibody to an internal protein of the SARS-CoV-2 rather than antibody to the viral surface spike proteins.[5]

**The Bad-** Using this test, the CDC reports that 57.7% of people (75% of children and adolescents) had been infected by Feb. 2022.[6]

**Vaccines: The Good-** Current vaccines were prepared from the original Wuhan SARS-CoV-2 isolate from 2019 and were available to almost all US adults by May 2021. The vaccines were all about 90% effective against the original Wuhan SARS-CoV-2 isolate and, at that time, the outlook looked good. 66.8% of the US population is fully vaccinated.[2] **Variants: The Bad-** Since then, there have been hundreds of viral variants with mutations in the surface S protein which make some more infectious. Dozens of variants were classified as variants of concern (VOC). At the same time, there has been a waning immunity in people vaccinated with the parent vaccine virus due to the mutations in the variant's surface protein epitopes which made them more infectious. Thus, it has become evident that there is a need for booster vaccines targeted at the mutant S proteins for the new, more infectious variant viruses. The Kaiser Family Foundation found that nearly 234,000 COVID-19 deaths in the United States could have been prevented "with primary series vaccination," Herd immunity seems unrealistic now due to the rapid generation of new, more transmissible SARS-CoV-2 variants, similar to what happens every year with influenza viruses. **The Good-** The good will be the rapid development of specific current SARS-CoV-2 variant vaccines and increased vaccinations.

**Disease: The Good-** Despite an increase in transmissible SARS-CoV-2 mutants, there was a decrease in diseases and deaths, but now, there is an increase in diseases, hospitalizations and deaths (5th spike?).

**The Bad- COVID-19 Pandemic:** The United States, the richest country with the best medical system in the world, has performed the poorest with this pandemic. We rapidly developed the first and best vaccines, yet due to political interference, internet misinformation, antivaxxers, and uneven medical coverages, we lead the world, by far, in total COVID-19 cases AND deaths due to COVID-19.[1,2]

**Long COVID:** The estimated global long COVID syndrome is 49%.[7] For patients that were hospitalized it is 54%, while it is 34% for outpatients with COVID-19. Their most common symptoms are fatigue 23%, followed by memory problems 14%, shortness of breath 13%, sleep problems 11%, and joint pain 10%. More women develop long COVID-19 than men (49% vs 37%, respectively).

**Brain Abnormalities:** There is also strong evidence for brain anomalies with reduction in grey matter thickness in the orbitofrontal cortex, reduction in global brain size, and cognitive decline over two time points.[8]

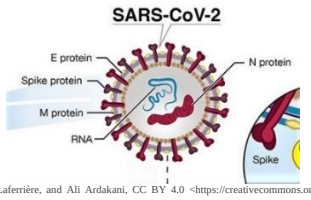
**US Life-span decline**: Life expectancy in the US declined 1.87 years during the

COVID-19 pandemic from 2019, more than any other peer high income country. Life expectancy declined on average only 0.58 years in all peer countries. In 2020, the average life expectancy in the peer countries was 81.50 years, 4.51 years longer than the 76.99 years in the United States.[9]

## Therapy:[10,11]

**The Good-** We have come a long way since the beginning of the pandemic and now have effective forms of therapy, both in hospital settings, and now, at home.[10,11] There are 2 classes of therapy: 1) against the SARS-CoV-2 virus: anti-viral therapy (convalescent serum, monoclonal antibody, anti-replication targeted chemicals) and 2) symptomatic COVID-19 disease therapy (steroids antipyretics, analgesics, and supplementary oxygen).

**Anti-SARS-CoV-2 therapy:**

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**Convalescent serum:** Convalescent serum contains neutralizing antibody against SARS-CoV-2. However, the WHO strongly recommends against convalescent plasma in patients with non-severe COVID-19.

**Monoclonal Antibodies (mAbs)**: Regional prevalence of variants of concern e.g., the regional prevalence of the Omicron BA.2 subvariant may affect which anti-SARS-CoV-2 monoclonal antibodies [mAbs] will be effective for treatment.

**Drugs- Antivirals:[10,11]**

**Paxlovid™ -ritinovir-boostered nirmatrelvir** WHO and NIH strongly recommend the use of Paxlovid in patients with non-severe illness at highest risk of hospitalization. Nirmatrelvir is an orally bioavailable protease inhibitor that is active against MPRO, a viral protease that is necessary for viral replication by cleaving 2 viral polyproteins. It has demonstrated antiviral activity against all coronaviruses that are known to infect humans. Paxlovid reduced the risk of hospitalization or death by 89% compared to placebo. **Paxlovid is the drug of first choice.**

An FDA panel recommends using Paxlovid orally twice daily for 5 days in those aged ≥12 years. Treatment should be started as soon as possible and within 5 days of symptom onset or a SARSCoV-2 positive test. Paxlovid has significant and complex drug-drug interactions. Before prescribing Paxlovid, clinicians should carefully review the patient's concomitant medications. **Paxlovid is a major breakthrough and gives hope for ending the pandemic.**

**Remdesivir** The FDA Panel recommends using remdesivir IV for 3 days. Treatment should be started within 7 days of symptom onset. Remdesivir should be administered where severe hypersensitivity reactions, such as anaphylaxis, can be managed. It is an option if Paxlovid is not available.

**Bebtelovimab** Bebtelovimab is a recombinant neutralizing human mAb, given by infusion. It binds to the spike protein of SARS-CoV-2. In vitro data suggest that Bebtelovimab has activity against a broad range of SARS-CoV-2 variants, including the Omicron variant and its BA.1, BA.1.1, and BA.2 subvariants. However, the FDA panel stated that Bebtelovimab should only be used if preferred treatment options are unavailable.

**Molnupiravir** Is an oral prodrug, a ribonucleoside that has broad antiviral activity against RNA viruses including SARS-CoV-2. The uptake by viral RNA-dependent RNA-polymerases results in viral mutations and lethal viral mutagenesis. As a mutagenic ribonucleoside antiviral agent, there is a theoretical risk that Molnupiravir will be metabolized by the human host cell and incorporated into the host DNA, leading to mutations. Molnupiravir is not as effective as preferred treatment options.

**Symptomatic Therapy:**

**Steroids** WHO strongly recommends systemic corticosteroids use in patients with severe and critical COVID-19, but not in patients with non-severe disease.

**Tocilizumab or sarilumab**- WHO strongly recommends these mAbs as IL-6 receptor blockers in patients with severe COVID-19 for their anti-inflammatory effects.

**Invermectin & Hydroxychloroquine- WHO strongly recommends against their use.**

## Animals- Spillbacks:

**Susceptibility:** Many animal species are susceptible to infection of SARS-CoV-2 from people (covered in our Newsletter "Animals and the COVID-19 Pandemic" Winter 2022, Vol. 21, No.1) and some can transmit the virus directly among their species. Now 4 animals, mink, mouse, deer, and hamster, are able to re-transmit the virus back to people (**spillback**).

**Mink:** Millions of minks have been infected from humans with SARS-CoV-2 and minks in many worldwide mink farms have been eliminated due to the **spillback** to humans.[12]

**Mink-Spillback**

**Hamster:** Occurrences of **spillback** from pet hamsters to their owners have been reported.[4] Also, 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 transmitted the virus back to people.

**Mouse:** **Origin of Omicron Variant- Mouse-spillback**[14]

The Omicron SARS-CoV-2 mutant was first found in South Africa on November 24, 2021. It spread rapidly throughout the world and is now dominant. It is much more transmissible than the original isolate. There is evidence that an earlier mutation, transferred from humans to mice sometime during 2020, mutated quietly as it spread among mice for over a year, before **spillback** to humans late in 2021 occurred. The authors did an elegant genetic study of the generation of numerous mutations in the S-protein of Omicron SARS-CoV-2 variants. The mutations occur in a pattern unique for each species of infected animal. They found the Omicron variants in people matched the pattern specifically from mice.[14]

**Deer:** Many white-tailed deer, in the USA and Canada, have high prevalence's of SARS-CoV-2 infections with several variants. A group found divergent lineage of SARS-CoV-2 in the deer with mutation signatures of host adaptation under neutral selection. There is an epidemiological link to a human case in the area which indicates **spillback,** deer-to-human transmission.[15] This is new evidence that mutants are being generated in deer which could make some more virulent for people.

## Commentary: Future of COVID-19:

**The COVID-19 pandemic is now endemic in the world. Dr. Tony Fauci reminds us that measles and polio still exist in the world, but are not endemic in the USA, due to vaccines. We will have to learn to live with COVID-19 just as we do with influenza viruses!**

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