

The Coronavirus Pandemic and Eosinophilia-Myalgia Syndrome

Stephen Naylor Ph.D.* & Gerald J. Gleich M.D.

*Address Correspondence to:

Dr. Stephen Naylor
Telephone: 812-272-0469
E-mail: lockett01@msn.com

1. INTRODUCTION

The world changed in 2020. The Eosinophilia-Myalgia Syndrome (EMS) community is now subject to another health-threatening problem. You have to deal with the vagaries of a miniscule particle known as the “coronavirus”. The scientific name of the virus is SARS-CoV-2 and the disease itself is known as Covid-19. This type of terminology is similar to that adopted for the Human Immunodeficiency Virus (HIV) that causes the disease Acquired Immune Deficiency Syndrome (AIDS). The scientific literature and media report that SARS-CoV-2 originated in the city of Wuhan, Hubei Province, China. Although new scientific analyses indicate that it possibly came from Shenzhen, Guangdong Province, China. Conspiracy theories notwithstanding, it has been suggested that the virus originated from the local bat population and was transferred to humans via another animal species like the pangolin (a scaly anteater). Chinese health authorities noted, in either mid-November or early December 2019 (the exact dates are disputed), that there were a small number of unusual infections in Wuhan. An alert was subsequently sent to the World Health Organization (WHO) on December 31, 2019.

The Chinese authorities shut down the city of Wuhan, but not before people from the city would travel widely both within China and across the globe. In addition there was limited understanding of what was occurring in the city of Shenzhen. The first case reported in the USA occurred on January 19, 2020 when a 35-year-old man was diagnosed in Washington State with Covid-19. Approximately two months later, (March 12, 2020), ~ (approximately) 20,000 infected patients and over 1000 deaths worldwide had been reported, and Covid-19 was designated a pandemic by the WHO. This was recognition that infectious agents such as viruses do not discriminate based on geography, race, or political persuasion. The SARS-Cov-2 virus is a simple ball of lipids (fat) encasing genetic RNA material, accompanied by 29 different functional proteins.

By June 14th, 2020, there were ~8.0 million people infected, and ~435,000 people had died across 185 countries. We are all observing, in real-time, the efficiency of this virus and the global damage and terror it can cause.

2. The Flu or Not the Flu, That is the Question?

All of you are familiar with the annual “Seasonal Flu” outbreak, which typically occurs from October-April in the USA. There are two types of human influenza/flu viruses, namely type A and B, along with associated subtypes (Note-the flu should not be confused with the common cold, caused primarily by members of the Rhinovirus family). Each year most of us get a “shot” which is a vaccine against the seasonal flu. The vaccine is not 100% effective because it is only a best estimate against the virus type/subtype that will be the infectious agent for the forthcoming year.

The deleterious effects of the seasonal flu virus on both individuals and populations vary from year to year. They are dependent on the infection efficiency, transmissibility, co-morbidity and mortality rates associated with the virus. We often regard this annual outbreak as an inconvenience, *but mistakenly, not life-threatening*. You should note however that in the 2018-2019 seasonal flu outbreak, an estimated ~35,000 people died and ~35 million people were infected in the USA alone. The previous year, 2017-2018, was much worse in the USA where ~61,000 died, and ~45 million were infected. On a global basis, it is estimated that ~250,000-750,000 die annually and over 500 million are infected with this “benign” seasonal flu!

SARS-CoV-2 is a member of a different viral family, the Coronaviruses. There are hundreds of viral species in this family. Human coronaviruses were first identified in the 1960's, and at present there are seven members of this sub-family known to infect humans. The most noteworthy includes the SARS-CoV-1 virus (origin-believed to be bats via civets to humans) that caused the outbreak of 2003 resulting in 8,422 infected individuals, with a fatality rate of

11%. In addition the MERS-CoV virus (origin believed to be from camels) caused an outbreak in 2012 that ultimately infected a total of 2,494 patients with a fatality rate of ~25%. There are no known vaccines available for either of these viruses.

The current virus that causes Covid-19 disease is a new threat that has not infected humans in the past. A significant consequence of this fact is that currently humans ***do not possess any immunity against the SARS-CoV-2 virus***. This is the primary reason why there has been such a massive global response to this infectious disease. The scientific and clinical communities are trying to rapidly learn as much as possible in order to understand the infection efficiency, transmissibility, co-morbidity and mortality rates of this new virus. What do we know so far? At present (June 15th, 2020), ~2.12 million Americans have been infected, and ~120,000 have died (representing a ~5.5% fatality rate). On a worldwide basis, ~8.0 million people have been infected and ~435,000 have died (~5.5% fatality rate). The SARS-CoV-2 virus appears to be more transmissible than the seasonal flu viruses. The estimates suggest that one infected person will infect 1.0-3.5 other people (seasonal flu estimates suggest one person infects ~1.5 other people). Fatality rate estimates range from 0.1-4.0% (seasonal flu ~0.1%), but this is still unclear and may change as testing dramatically increases, and the accuracy of diagnosing individuals infected with SARS-CoV-2 is improved. It should be noted that a small pilot study (with significant limitations) in NY State suggests infection rates of up to 20% of the population. A common co-morbidity between SARS-CoV-2 and seasonal flu is the onset of Acute Respiratory Distress Syndrome–like symptoms, attributable to the striking ability of the virus to infect the lung and decrease its function. The incubation period for SARS-CoV-2 after infection is 2-14 days (average-5 days). In contrast, seasonal flu incubates for 1-4 days (average-2 days). Symptoms for both Covid-19 and seasonal flu are very similar, and include fever, dry cough, fatigue, lack of appetite and shortness of breath. Note that the CDC recently announced new symptoms for Covid-19 that include chills, muscle pain,

headaches, sore throat and loss of taste /smell. All these data clearly indicate that SARS-CoV-2 is a virus that causes a flu-like disease, with pronounced similarities to the seasonal flu.

This perplexing virus however, also appears to possess other infective properties that make it different from both the seasonal flu as well as from the SARS-Cov-1 coronavirus of 2003. A series of unusual symptoms associated with SARS-Cov-2 infection have been reported. They include i) Covid Toe - a skin rash on toes similar to chilblains, and rash on the sole of the foot; ii) conjunctivitis (commonly referred to as pink eye); iii) skin necrosis- a red or purple mottled pattern due to a lack of blood supply; iv) dizziness/headaches; v) tingling or burning sensation, probably due to your immune response. In addition, numerous reports have now appeared in the literature indicating that many patients suffer from abnormal clotting of the blood. This can lead to problems throughout the body depending on the location of the clot and can produce conditions such as an ischemic stroke. Finally in both the UK and USA, a condition similar to Kawasaki disease (over-active immune response) has manifested in babies and young children, and tragically a baby recently died due to this SARS-Cov-2 related co-morbidity. Recently the CDC announced that this condition should be diagnosed as “Multisystem Inflammatory Syndrome in Children” (MIS-C).

3. Prevention and Treatment of SARS-CoV-2

EMS patients have additional factors to consider in this Covid-19 pandemic. Such individuals typically possess compromised immune systems as well as other damaged organ problems caused by the original elevated eosinophil levels. All EMS patients need to take additional precautions against SARS-CoV-2 and should consider the following:

i. Prevention- The SARS-CoV-2 virus can be spread directly from human-to-human through the air via water droplets or aerosol transmission. Recent data have indicated that an infected individual coughing or sneezing out viral particles

can spread the infectious agent over 12-27 feet. This is a much greater distance than the 6 feet physical distancing recommended by the Centers for Disease Control and Prevention (CDC). Also studies have demonstrated that the virus can stay airborne for up to 8 minutes in certain circumstances. In addition the virus can also be transmitted by physical contact with a contaminated surface. Studies suggest that the virus can survive several days (1-7 days) depending on the type of surface material, such as cardboard, plastic or metal.

In order to minimize physical exposure to the virus individuals should follow guidelines suggested by many states to “shelter-in-place” or “stay-at-home”. If you must venture outside to purchase groceries or medications or to exercise, then you should consider the following. The virus must enter your body to actually infect you. This transmission is primarily thorough your mouth, nose or eyes by direct contact with virus containing water droplets or an aerosol. A secondary route is when your hands touch a contaminated surface and then you touch your face. So when you venture outside, wear a facemask and wrap-around glasses to cover your mouth/nose and eyes, respectively. This should significantly reduce airborne infection as well as prevent you touching your mouth, nose and eyes with contaminated hands. In addition, wear disposable gloves. This latter action does NOT prevent picking up the virus from contaminated surfaces, but you must immediately and safely discard the gloves on arriving back at your home before touching your door handles. Once in the home, immediately wash your hands for 20-plus seconds, and insure washing between fingers and your thumbs. You should take a shower to remove any residual virus from your body. Finally in terms of home delivered food and other packages; i) if possible avoid restaurant prepared foods and make your own meals, ii) wipe down cardboard or Styrofoam box surfaces with hand wipes.

ii. Therapeutic Options - EMS patients need to consider the role of elevated eosinophils, organ damage caused by eosinophilia, and compromised immune system function.

a. *Immune System*: “The essential is invisible to the eyes,” writes Antoine de Saint-Exupéry in his novella *Le Petit Prince*). Your immune system is a complex host defense system consisting of a myriad of components and processes. Without it, we all would die. A compromised immune system results in greater susceptibility to infectious pathogens such as SARS-CoV-2. The *innate* immune system contains white blood cells such as the eosinophil and the neutrophil. Eosinophils target and kill parasitic infections, whereas neutrophils neutralize invading bacteria and viruses. Our *adaptive* immune system consists of B-cells and T-cells responsible for the production of antibodies and subsequent removal of most foreign particles, including a splinter or a virus. A normal, responsive immune system serves to protect you against agents such as SARS-CoV-2.

Individuals with compromised immune systems can more easily be infected and struggle to overcome the infectious agent. Thus, it is important to take steps to strengthen your immune system. Many EMS epidemic patients have already incorporated such steps into their daily, healthy lifestyle practices. These include: do not smoke; do consume a diet high in fruits, vegetables and nuts; get regular exercise; manage weight and alcohol consumption; get adequate sleep; and try to manage stress. See - <https://www.health.harvard.edu/staying-healthy/how-to-boost-your-immune-system> for more details. In addition follow the advice of your physician and consider the adoption of diet and/or medication that work against oxidative stress and systemic inflammation.

b. *Drug and Antibody Therapies*: This is an active area of research, discovery and development, and somewhat clouded by misinformation. According to clinicaltrials.gov there are currently 524 ongoing trials for SARS-CoV-2 diagnoses and treatments. In addition there are ~160 drug therapies and 102 vaccines being evaluated at the present time. HOWEVER, TO BE CLEAR THERE IS ONLY ONE DRUG, REMDESIVIR (GILEAD), APPROVED BY THE FDA FOR THE TREATMENT OF COVID-19 AT THIS TIME. (This drug reduces

the amount of time a patient needs to spend in the hospital.) The process that a candidate drug must go through to be approved is both rigorous and very time-consuming. There are regulatory shortcuts that can be implemented in certain circumstances such as a pandemic. However, these systematic steps have been put in place to protect the public and insure that drugs are both safe and efficacious for the disease treatment approved.

A drug that has received massive misplaced media attention is Hydroxychloroquine (HCQ). This drug was approved in 1955 for the treatment of malaria and has also been approved for the treatment of lupus and rheumatoid arthritis. It has a number of adverse side effects including sudden cardiac death. Some promising cellular studies in the early 2000's suggested HCQ might be useful against coronaviruses. More recently, a few small, poorly designed human studies appeared to indicate that HCQ might prevent infection and alleviate symptoms of SARS-CoV-2. These very preliminary studies prompted the President of the United States to unwisely trumpet the potential of this drug in the treatment of Covid-19. Indeed, the FDA has issued an order that physicians can write a prescription for off-label use of HCQ against SARS-CoV-2 in an emergency. However, the dilemma is that comprehensive data is not yet available on the safety and efficacy of HCQ in Covid-19 treatment. The small number of recent, well-designed studies has provided contradictory results. Also human trials in both Sweden and Brazil were *stopped* due to adverse heart complications in clinical trial patients! In addition, the US Veterans Administration just announced the results of a trial of 368 patients. This and other studies have all found NO advantage to the use of HCQ for treating Covid-19. Indeed, in the Veterans Administration study, more patients died compared to the control group. While there are still now ~80 ongoing clinical trials of HCQ (with or without Azithromycin) involving thousands of patients, this drug has fallen out of favor. Data from a number of large scale clinical trials now indicate that HCQ is NOT effective against SARS-CoV-2 in the treatment of Covid-19.

As noted above, another more promising approach is the repurposing of the Gilead pro-drug, Remdesivir, against SARS-CoV-2. This drug was evaluated and used in the 2014 Ebola outbreak that occurred in the USA. A recent study of 61 Covid-19 infected patients showed that 68% of participants receiving the drug manifested improved clinical outcomes. The FDA recently approved its use in Covid-19 patients. Another promising avenue of enquiry is the use of blood plasma from patients who have “recovered” from a SARS-CoV-2 infection. These patients produced antibodies (from their adaptive immune system) against the virus while infected. In a study from April 6, 2020, ten severely ill patients infected with SARS-Cov-2 were given a single dose of 200 mL of plasma from recovered individuals. The “clinical symptoms were significantly improved” in patients receiving the plasma/antibodies and “no adverse side effects were observed”. The authors caution that much more work is needed to optimize dosing and to insure efficacy and safety in a larger population of patients. But these initial data afford hope without the hype.

c. *Vaccine*: This is the gold standard treatment of viral infections. Almost all of us have been subject to vaccination including measles when younger. Vaccines contain the actual infectious agent that causes the disease. The difficulty is to ensure that the vaccine does not harm the recipient, but elicits an immune response to produce antibodies against the pathogen. In order to achieve this goal, the patient can receive a dead or weakened, less virulent infectious pathogen. More recently, new approaches using specific regions of DNA or RNA from the pathogen have been used in order to further minimize the potential of the vaccine causing infection in the patient. The considerable advantages of vaccines are that they actually prevent the infectious agent pathology, without the danger of the patient becoming sick. In addition, the vaccine confers some immunity that can last months to years for the patient. Currently, there are 106 ongoing clinical trials worldwide for a vaccine against SARS-CoV-2. The development of a vaccine typically can take several years. But, given the exigent

circumstances, there are claims that in this case it may only take 9-18 months. There have been some overly optimistic statements that a vaccine might be available by the end of the year!

4. Summary

We are all in uncharted waters of uncertainty. Much of this is due to our lack of innate and adaptive immunity against SARS-CoV-2. To combat the pandemic our local, state, federal and global governments/agencies have made dramatic and impactful changes to our daily lives. In addition, we are all trying to ascertain what to do! Should we wear masks or not? Should we take HCQ to prevent or treat Covid-19? Should we stay home or mix freely with friends and coworkers? This continues to be an evolving situation, and all of us should filter information from a variety of sources in order to best judge what is optimal for one and all. As we learn more about SARS-CoV-2, history will determine if what we have been told to do was an over-reaction or a conservative response by prudent governments/agencies and each one of us. Time will tell.

At the present time, given what we know, what can EMS patients do? This is particularly pertinent as the USA begins to try and open up again. A history of elevated eosinophils will not directly cause an individual to be more susceptible to SARS-CoV-2 infection. However, the consequences of chronic elevated eosinophil levels may have caused organ damage, impaired immune response and systemic inflammation, thus leading to enhanced infection susceptibility. Given the compromised immune systems and damaged organs of many patients (both due to EMS itself and also to the treatments for the disease), plus the lack of a vaccine, prevention is the best option currently available. Individuals should stringently practice physical distancing and adhere to shelter-in-place guidelines. Follow the medical advice only of your physician as it pertains to potential therapeutic treatments. This is particularly important at the present time given

that the President of the USA just appeared to suggest that you administer a known toxin, namely disinfectant, to yourself for treating Covid-19!

(Please note the opinions expressed in this article are solely those of the authors and do not necessarily reflect the views of NEMSN. Readers should consult with their personal physicians as to how to manage the prevention and treatment of Covid-19 flu.)

Dedication

We would like to dedicate this article to all original EMS epidemic patients from the 1989-1990 outbreak. Your quiet fortitude, good humor and constant willingness to fight and not give up have been remarkable. Wendy Rosenblatt was one such individual who manifested the epitome of this dignified fighting spirit. Wendy died a year ago due to complications from EMS. One of us (SN) got to know Wendy through numerous conversations in the last two years of her life. Like most of you, she fought her myriad of complications from EMS with humor, love of family, and a never-give-up attitude. As Covid-19 sweeps the globe, current frightened and panicked SARS-CoV-2 infected patients can learn much from all of you.

Useful Covid-19 Links

1. World Health Organization (WHO)- Details on worldwide pandemic.
https://www.who.int/health-topics/coronavirus - tab=tab_1
2. Centers for Disease Control and Prevention (CDC)- USA perspective.
<https://www.cdc.gov/coronavirus/2019-ncov/index.html>

3. Mayo Clinic - medical details.
<https://www.mayoclinic.org/diseases-conditions/coronavirus/symptoms-causes/syc-20479963>
4. WebMD - symptoms
<https://www.webmd.com/lung/covid-19-symptoms>
5. National Institutes of Health PubMed (NIH) - Scientific literature access, search engine. <https://pubmed.ncbi.nlm.nih.gov/>
6. Johns Hopkins University - Global and Regional Coronavirus Tracker-live.
<https://coronavirus.jhu.edu/map.html>