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# Assessing for the Co-morbidities and Factors That May Affect a Patient's Risk and Response to COVID-19

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**Abstract:** The COVID-19 pandemic has impacted every country in the world and every aspect of how we live. A number of comorbidities and characteristics have been associated with increased risk of mortality for those that contract COVID-19. Naturopathic doctors have an essential role to play in supporting public health's policies around prevention and in assessing for and addressing factors that may contribute to increased risk. It is also critical that the naturopathic profession understand the characteristics of SARS-CoV-2 and the potential long-term impacts on health for those that have had the virus. This article reviews the current research around COVID-19 and highlights the laboratory testing that may be indicating when assessing for risk and the symptoms that patients may present with post-COVID that may need to be addressed.

## Introduction

In December 2019 in Wuhan, China, Province of Hubei, patients began lining up outside of hospitals with a mysterious illness. In late December China notified the World Health Organization (WHO) of this new, serious respiratory infection. On March 11, 2020, the WHO declared a global pandemic now known as SARS-CoV-2 or COVID-19 as the virus had spread to Japan, South Korea, Iran, ski resorts in Italy and Austria, and across the balance of Europe and North America.[1] It was labeled SARS-CoV-2 as the first coronavirus that emerged in late 2002 which caused severe acute respiratory symptoms was referred to as SARS-Co-V or in some cases SARS-CoV-1. The SARS-CoV-1 pandemic ended in June 2003 with a total of 8098 reported cases globally, 774 deaths, and a fatality rate of 9.7%; including some 250 cases and 38 deaths in Toronto, Canada.[2] A related respiratory virus also caused by a coronavirus was the Middle East Respiratory Syndrome (MERS-Co-V) which emerged in 2012 and resulted in 2494 reported cases with 858 deaths across 27 countries and had a fatality rate of 34%. MERS-Co-V was common in dromedary camels and zoonotic cases continue to occur.[3] The current SARS-Co-V-2 appears to be less deadly, but more transmissible. As of September 4th, 2020, the global count is over 26 million cases and 864,000 deaths with a global fatality rate of about 3.3%.[4] Genetically SARS-Co-V-2 is 79.6% similar to SARS-CoV-1 and 96% like bat corona virus.[5] As of yet, there is no successful coronavirus vaccine, although there were many attempts for SARS-CoV-1 and MERS-Co-V.[6]

The majority of people that contract COVID-19 are believed to recover on their own. Although there are certain substances and procedures that are in current use to ease COVID-19 symptoms, there are currently no vaccines, drugs or substances either in conventional health-care or in the realm of Traditional and Complementary Medicine (T&CM) recognized by the Canadian government as effective in treating COVID-19.[4,7] There is a growing number of research studies and clinical trials being conducted around the world with the aim of helping the global healthcare community understand SARS-CoV-2 and how to prevent and treat those affected. The WHO website on COVID-19 includes 18 established research resources including the *Lancet, Jama* and Elsevier that provide open-access to the research on COVID-19.[8] During this global pandemic we have seen unprecedented collaboration and sharing of research findings. With the aim of having naturopathic treatments considered as viable options in the management of COVID-19, the World Naturopathic Federation (WNF) worked with over forty naturopathic researchers, practitioners and content experts around the world to complete ten rapid reviews. Table 1 highlights the rapid reviews that have been completed to-date. These rapid reviews have been published individually and as a special open-access issue of the scientific journal *Advances in Integrative Medicine* (Elsevier).[9]

What is becoming clear is that COVID-19 is here to stay, at least for the next few years. Naturopathic doctors in Canada and other parts of the world have been restricted by governments and regulators to treat COVID-19.[10] However, naturopathic doctors have a key role in working with patients to address the co-morbidities that are associated with increased risk of serious disease and mortality, to help patients manage the tremendous mental-emotional strain this pandemic is having on them and their families, and to work with patients that have had, or believe they had, COVID-19 and are experiencing residual health effects. With the dissemination of the rapid reviews conducted by the WNF, there is reason to suspect that naturopathic treatments and other T&CM treatments will be given consideration by the global healthcare world in the management of COVID-19.

This practice-based article provides naturopathic doctors with an understanding of COVID-19. It outlines what we currently know about the virus, it discusses some of the questions that have been raised about COVID-19 and how it affects organ health and it highlights those laboratory tests to consider when assessing a patient's increased risk for the co-morbidities associated with COVID-19 and for those patients that continue to have symptoms after experiencing COVID-19.

## What We Know About COVID-19

### *Symptoms*

According to the WHO, about 80% of patients that contract COVID-19 have mild symptoms or are asymptomatic. For those that have symptoms, they can range from mild, moderate to severe with a high degree of variability amongst patients.[4] The most common symptoms include a fever of 38.1°C or greater; cough or worsening of a chronic cough; shortness of breath; difficulty breathing; diminution, loss of sense of taste or smell or altered taste or smell; chills; headaches; unexplained fatigue, malaise; muscle aches or myalgia; nausea, vomiting, diarrhea and/or abdominal pain; pink eye or conjunctivitis; and runny nose, nasal congestion without a known cause such as allergy.[11-13] Morbidity and mortality are higher in individuals 60 years old and above, based on data from China, South Korea, Italy and elsewhere.[13-16] There is a lot of overlap between COVID-19 and the common cold or influenza, but the symptoms that are unique to COVID-19 include a loss of taste and smell, and early symptoms of serious disease including decreased oxygen saturation.[17, 18]

### *Susceptibilities To Contracting COVID-19*

Who is at risk of contracting COVID-19 has changed since the onset of COVID-19 and is influenced by the testing that is being done. Individuals with underlying conditions such as diabetes type II, cardiovascular disease (CVD), cancer, chronic kidney disease, chronic obstructive pulmonary disease (COPD) and obesity or BMI >30 appear to be at the greatest risk of severe symptoms or increased mortality if they contract COVID-19.[11,12] According to the US Centers for Disease Control and Prevention (CDC), individuals with underlying conditions are 6 times more likely to be hospitalized and 12 times more likely to die compared to those who have no such conditions.[19] As of May 30, 2020, 1,761,503 cases and 103,700 deaths had been reported to the CDC, with 1.3 million included in the analysis and data on underlying health conditions available for 287,320 (22%) of which 198,979 had one or more other conditions and 88,441 had none. 45.4% of those with cardiovascular disease or diabetes were hospitalized versus 7.6% without an underlying condition. 19.5% of COVID-19 patients with underlying conditions died compared to 1.6% with no underlying condition and among ICU (intensive care unit) admissions the rates were 8.5% and 1.5%, respectively.[20] Another susceptibility factor may be age, especially when there are comorbidities.[21] Confirmed cases in the USA were 902 per 100,000 for 80 years old and up, and 550.5 per 100,000 for 50-59 years old.[22] Social determinants of health such as employment, housing, socioeconomic status, health care access, and racism are also factors that appear to impact infection rates. In a CDC study of those diagnosed with COVID-19, 33% were Hispanic, 22% Black and 1.3% were Native American /Alaska Native; yet these people accounted for 18%, 13% and 0.7% of the USA population, respectively.[23] Also those individuals that are Native American are reported to be 5.3 times more likely to be hospitalized compared to Caucasians, Blacks 4.7 times and Hispanics or Latino individuals are 4.6 times more likely. Likewise American Indian are 1.4 times more likely to die if they get COVID-19 compared to Caucasians, Blacks are 2.1 times more likely, and Hispanic or Latino individuals are 1.1 times more likely.[11] These differences are a concern in some countries such as the United States as Hispanic health aid workers represent 17.1% of the entire health aide workforce.[23]

Although males appear to have a high mortality rate, this difference may be due to lifestyle factors more than biological sex differences.[19, 21]. In a *Lancet* study published in August 2020, the overall male to female mortality sex ratio per 100,000 population in European countries was reported as 1.4.[21] The higher mortality rate in men may be tied to higher baseline IL-8, IL-18 and CCL5 compared to women and a more robust T-cell response in women.[24] For people aged 0–9 years, the ratio was 0.81, a ratio of 1.9 in the 40–49 age group, 2.3 in the 50–59 year age group, 2.6 in the 60–69 years age group, and 1.65 in people older than 80 years.[21.]

In the news there has also been reports of medications that have been associated with an increased risk of severe reaction or mortality to COVID-19. Two medications that have been studied are ACE inhibitors and proton pump inhibitors (PPI). The research on ACE inhibitors is varied. Some studies have indicated that patients on ACE inhibitors are at greater risk, others indicate that they are not.[25] The data on the use of PPIs , however, is quite clear. In a survey of 264,058 persons of whom 86,602 completed the survey, 6.4% reported testing positive for COVID-19. Those who took a PPI up to once a day were twice as likely to report having a positive COVID-19 test as those who did not (OR 2.15; 95% CI 1.9-2.44). Those who took the PPI twice per day were almost 4 times (OR 3.67, 95% CI 2.93-4.60) as likely to test positive for COVID19. However, those who used an H2 receptor antagonist once per day were 15% less likely to report a positive COVID-19 test (OR 0.85; 95% CI 0.74-0.99).[26]

An additional risk factor may be blood type. Some studies indicate that blood type A has the greatest risk, whereas other studies indicate that it is blood type AB or B. While these blood types are inconsistently associated with increased risk, blood type O appears to be consistently associated with a lower risk.[27, 28] For example, an examination of blood type in 2173 COVID-19 confirmed patients from Wuhan and Shenzhen, China, found a lower risk with blood type O, $p<0.001$.[27] Similar result were found among 775 patients and 950 controls from Spain and 835 patients and 1255 controls from Italy.[29] What is interesting about this data is that those with blood type O were also less likely to be infected by the SARS-CoV-1 virus.[30]

### *Stages Of COVID-19*

There are four stages associated with COVID-19: prevention, infection, escalating inflammation and recovery.[31] Public health focuses on measures such as social distancing, hand washing and wearing of masks as preventive measures. Naturopathic practice follows the guidelines set by Public Health for prevention and includes a number of health promotion strategies as well. When a person contracts COVID-19 it generally starts as an upper respiratory tract infection which binds to target cells, similar to SARS-Co-V-1, through the angiotensin-converting enzyme-2 (ACE-2) receptor which is expressed by epithelial cells of the lung, intestine, kidney and blood vessels.[32] The ACE-2 receptor is more likely to be expressed at higher levels in type 1 or 2 diabetics and those treated with ACE-inhibitors and angiotensin II type-1 receptor blockers (ARBs) which up-regulate ACE-2.[31] ACE-2 can also be increased by use of thiazolidinediones and ibuprofen as well as in lung diseases, cancer, and hypertension, but not by calcium channel blockers.[33] From the respiratory tract, COVID-19 can descend into the gastrointestinal tract, kidneys, and the individual's vasculature affecting different organ systems and causing multiple and diverse coagulopathy such as disseminated intravascular coagulation (DIC) often with dire consequences depending on which organ systems are attacked by the virus.[34] As the virus progresses to the inflammation stage, the result can be significant elevations in fibrinogen, hsCRP, and d-dimer and can lead to pulmonary vasculopathy.[33]

Another organ system where symptoms can develop are the skin, especially in children, with chilblains or Kawasaki-like disease. The symptoms that manifest include non-purulent conjunctivitis, polymorphic rash, mucosal changes, swollen extremities, and in some cases shock and coronary artery aneurysms. This has also been labeled as pediatric inflammatory multisystem syndrome (PIMS).[35, 36]

### *Testing for COVID-19*

Reverse Transcription Polymerase Chain Reaction (RT-PCR) is the gold standard for diagnosis of COVID-19. RT-PCR may be positive with variable predictive value during the infection period, early infection, active phase of infection, and in the late and recurrent stages of infection. The optimal time for testing is in the first days after symptoms emerge. False negatives are more prevalent during the presymptomatic stages and during the recovery stage of the infection. It's important to note, however, that PCR tests can also remain positive long after individuals are no longer contagious.[37]

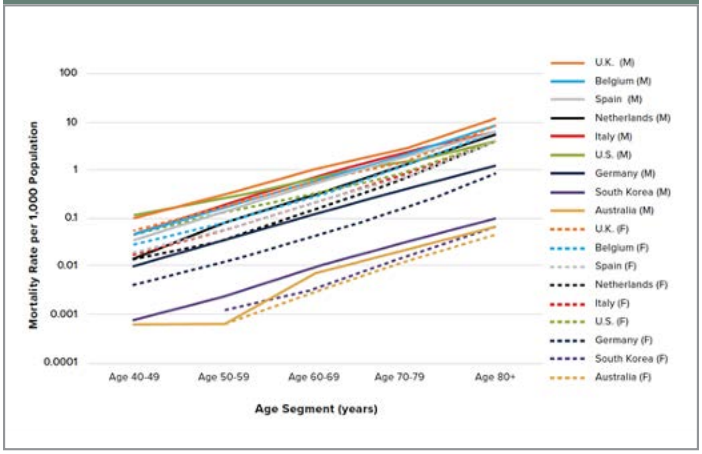
Antibody testing can be used to determine if an individual has had COVID-19, yet the timing of testing is critical as antibody detection is accurate 30% at one week, 72% at two weeks and 94% at three weeks.[38, 39] Typically IgM values are initially elevated in 5-7 days followed by elevation of IgG values at about 3 weeks. IgG levels were significantly lower in asymptomatic compared to symptomatic individuals (p-0.005) and median duration of viral shedding was significantly longer in the asymptomatic group, 15-26 days (p=0.028), therefore indicating a weaker immune response to COVID-19.[39] It is important to note that at the time of writing there were no approved antibody tests for use in Canada.[40]

### *Risk and Mortality Rates*

Healthcare workers appear to have a higher mortality rate when infected by a coronavirus. Mortality rates for SARS-CoV-1 in Guangdong, China, as of November 2002 were 10% among the general population and 23.1% among health-care workers. Similarly for COVID-19 in Wuhan, China, the population mortality was 2.9% while among health-care workers it was 16%.[41] The high death rate among health-care workers is assumed to be due to repeated virus exposure, exposure to multiple strains, high doses with each exposure, and re-infection over a shorter period of time.

Death rates increase with age as shown in Figure 1.[42] The highest rates are in individuals aged 70-80 plus in all countries. In Italy and Germany, male mortality has been 2.5 to 3.5 times that of female mortality in all except those 80-years-old or greater. The cause of higher male mortality was initially thought to be because more men than women smoke, but that finding does not hold in Italy where smoking rates by sex are nearly equal. The tendency for increased mortality in males is similar to what was seen in the 2003 with the SARS-CoV pandemic in Hong Kong where mortality rates were 22.3% for males and 13.2% for females, and in mice infected with SARS-CoV males were much more susceptible suggesting that sex differences in immune response may be a factor, or it could be as simple as compliance with handwashing and other protective measures in humans.[42]

**FIGURE 1: Death rate by age and country.[42]**




## Addressing Susceptibilities

Health promotion is a central tenet of naturopathic care and involves addressing a patient's susceptibilities and risk factors. Due to the correlation of increased severity of COVID-19 associated with certain comorbidities, it is reasonable for naturopathic doctors to address the nutrient deficiencies, lifestyle factors and environmental factors that are known to be associated with these comorbidities. It is not about the promise of being immune to the virus, it is about ensuring that each person is as healthy as they can be for the health challenges that they may face.

### *Nutrient deficiencies*

Nutrient deficiencies are associated with diabetes and cardiovascular disease and other co-morbidities associated with COVID-19.[43-45] Specific nutrient deficiencies such as vitamin A, vitamin B12, vitamin C, vitamin D, zinc, omega 3 fatty acids, as well as lower levels of glutathione, and melatonin can impact immune and inflammatory responses.[31, 46] Although there is an absence of high quality, contemporary clinical research to support the therapeutic use of these nutrients in reducing symptoms associated with acute respiratory infections, the following is a quick overview of the findings from rapid reviews conducted by the WNF:

- Vitamin C may improve respiratory function and decrease the severity of respiratory infections. It is an essential micronutrient involved in various cellular functions of both the innate and adaptive immune system and it has powerful antiviral properties by the way of increasing Natural Killer (NK) cells.[47]
- Vitamin D deficiency is associated with an increased risk of acute respiratory tract infections.[48] A number of the co-morbidities for COVID-19 are also associated with deficiencies in Vitamin D, including obesity, diabetes type II and cardiovascular disease and hypertension.[49-50]
- Zinc is essential in many aspects of infection and inflammatory healing processes. Research indicates that zinc may potentially decrease the risk, duration and severity of acute respiratory infections, particularly for people at risk of deficiency.[51]
- N-acetyl cysteine (NAC), administered intravenously, may help improve outcomes in people with acute respiratory distress syndrome and may assist in improving markers of inflammation or oxidation.[52] NAC is needed to make and replenish glutathione. Glutathione is one the body's most important antioxidants involved in the regeneration of vitamins C and E. Glutathione deficiency, often correlated with low vitamin D levels, may be an important underlying factor leading to serious COVID-19 infections.[53]
- Melatonin has antioxidant properties as well as speculative antiviral and anti-inflammatory effects[54,55] Melatonin levels naturally decrease with age, but they are also affected by a person's adherence to the natural circadian rhythm. Sunlight stimulates the production of serotonin which is a precursor to melatonin. Daylight exposure in the elderly and appropriate sleep hygiene lead to better sleep and higher melatonin production.[56]

### *Lifestyle Factors*

There are several lifestyle factors that are known to be associated with respiratory health and with inflammation management. [31] Although research evidence is lacking to show the benefit of lifestyle changes on either the infection rate or clinical outcomes of COVID-19, SARS-CoV-2 is a reminder of the importance of addressing diet, sleep, stress management, movement, and other lifestyle factors where possible to help with general health promotion and to assist in the prevention and management of chronic non-communicable diseases where possible.

- **Diet** is an aspect of lifestyle that most naturopathic doctors assess.[57] Historically a well-balanced diet with a focus on fresh fruits and vegetables, lean protein and whole grains as well as adequate hydration was believed to provide the required nutrients for health and healing.[58] Although research is lacking to support these recommendations, there is data to suggest that ultra-processed foods do increase mortality risk in multiple countries.[59]
- **Sleep** is increasingly becoming recognized as essential to immune health.[31] The body heals optimally during deep sleep and sleep itself can have an anti-inflammatory effect.[60] Short sleep, disrupted sleep and even prolonged sleep are associated with decreased immune function.[61,62]
- **Movement** is important for immunity. As this virus is affecting respiratory health and oxygen-carrying capacity it is very important to remind patients that movement on a daily basis is associated with a decreased risk of respiratory infections and a decreased risk of infections becoming severe.[63]
- **Breathing** is essential to life. The ability to take a deep, full breath is an indicator of overall respiratory function.[64]
- **Time outside** helps to provide the skin exposure to the sun and thus the production of vitamin D, which is essential to immune health. It can also increase the activation of T-cells resulting in a faster immune-response.[65]

### *Co-morbidities*

As discussed, the co-morbidities that have been associated with an increased risk of severity or death due to COVID-19 include diabetes, cardiovascular disease and chronic inflammatory states.[11,12,19] In June of 2020, it became clearer that SARS-COV2 targets the vasculature, affecting the cardiovascular system as well as the respiratory system, involving physiological processes related to oxidative stress, reactive oxygen species, inflammation and disruption to the endothelial membranes of blood vessels.[66]

Table 2 outlines some baseline laboratory testing that may assist in identifying any underlying co-morbidities that may be addressed by naturopathic care. Key points include:

- HbA1c is a 4-month measurement for blood sugar control and is diagnostic for diabetes, as well as a marker for identifying people at high risk.[67]
- Creatine kinase (CK) assesses for muscle damage. CK-MB is specific for heart muscle. Brain natriuretic peptide or proBNP is often used as part of an assessment for a cardiovascular event, but it may also be used as marker for overall heart health and blood vessel health, particularly if heart failure or aneurysms are suspected.[68]
- CRP indicates general inflammation within the body, whereas hs-CRP is inflammation associated with cardiovascular blood vessels.[68]
- A CBC is often association with assessing for infection, yet a high WBC can indicate inflammation, especially if the neutrophil to lymphocyte ratio is above 3.[69]

## COVID-19 and Chronic Inflammation

What is the most concerning about SARS-CoV-2 is that the deleterious effects are less about the rate of viral replication and more about the level of inflammation that is caused by the virus. Inflammation is an active and passive complex process impacted by many factors including nutrient levels, the extracellular matrix, the presence of inflammatory signaling molecules and genes, the microbiome, epithelial barrier health, lifestyle and other factors.[31,70]

The SARS-CoV-2 virus attaches to the epithelium of the lung with spike proteins on the ACE2 receptor.[32] The lungs, blood vessels, heart, kidney and digestive system all have ACE2 receptors on their endothelial barriers. As the viral load increases the virus produces the enzyme 3CL protease which inhibits a person's innate immune response and allows the virus to spread to the ACE2 receptors in other organs, disrupting cell integrity and altering organ function.[32]

Ideally, the inflammatory response resolves on its own, but in a subset of people, inflammation continues to amplify, and may result in endothelial damage that can cause scarring, fibrosis, organ damage, autoimmunity and even death.[70] In the media, people who report prolonged symptoms associated with COVID-19 are often referred to as 'Long Haulers".[71,72] Chronic symptoms reported by people diagnosed with COVID-19 include shortness of breath, extreme fatigue, difficulty concentrating, brain fog and a variety of other symptoms depending on the person.[73]

Post COVID-19 organ damage can affect many different organs, but has an affinity for the liver, heart, kidneys and brain. The three stages of neurological sequelae associated with COVID-19 include:

- NeuroCovid Stage 1: Damage due to the virus is limited to the epithelial cells of the nose and mouth. The main symptom is a loss of smell or taste. It is important to note that acute loss of smell is a significant prognostic symptom indicating COVID-19.
- NeuroCovid Stage 2: Cytokine storm that begins in the lungs travels in the blood vessels to all body organs. Results in the formation of blood clots and causes small or large strokes in the brain.
- NeuroCovid Stage 3: An overactive cytokine storm damages the blood brain barrier and virus particles invade the brain. The result is seizures, confusion, coma or encephalopathy.[74]

Assessing for the impact of organ changes may be considered for any patient whose symptoms haven't resolved after being ill with a confirmed case of COVID-19 or an undiagnosed respiratory infection. When you examine the laboratory findings of those that have severe COVID-19 symptoms or those that have died as a result of COVID-19, the results resemble what you would expect to see when patients die of a cardiovascular events, such as a heart attack or a stroke with high values in ALT, LDH, CK-MB, D-Dimer, hs-CRP and ferritin, along with leucopenia and lymphopenia.[75] When you have patients that report "never being well since a known or suspected case of COVID-19", it is the opinion of the authors that it would be prudent to run laboratory tests to assess for chronic inflammation, kidney and liver health status, cardiovascular health and hypoxia. Table 3 outlines the key post-COVID-19 laboratory tests to consider. Some highlights include:

- ALT is more specific for liver or heart disease whereas AST is more specific for hepatitis, trauma and alcoholism. A high ALT/AST ratio indicates liver damage. High ALT along with elevated LDH and CK-MB indicates increased risk of a cardiovascular event.[76]
- When ferritin levels are very high they may indicate congestion in cerebral blood flow, chronic inflammation or disease, elevated iron intake, liver disease or hemochromatosis.[77]
- The laboratory indicators that demonstrate the highest risk of mortality include an increase in D-dimer, high ferritin or lactate dehydrogenase (LDH) levels or a progressive decrease in lymphocytes over time[78]
- Signs of ongoing inflammation include high hs-CRP, ferritin and/or ESR. In-office testing of oxygen saturation can also be an efficient way of detecting those patients with 'silent' hypoxia. Pulse oximeter readings below 95% can indicate a high risk of mortality and the need for referral to emergent care for further investigation.[79]

## Conclusion

Patients will be visiting naturopathic doctors expecting them to provide medical advice related to COVID-19. Patients will be looking for support with respect to overall immune and mental health, ways to address co-morbidities associated with increased risk of COVID-19, advice related to supportive measures or because they are concerned that they had or suspect they had COVID-19 and have not felt well since. Although naturopathic doctors in Canada, at this current time, cannot directly treat patients with COVID-19, it is imperative that they stay informed of the physical and mental impact on patients and how to properly assess for them. Laboratory testing is an essential tool as part of a thorough assessment.

**TABLE 1: World Naturopathic Federation Rapid Reviews**

| RAPID REVIEWS |
|---|
| Vitamin C |
| Vitamin D |
| Zinc |
| Quercetin |
| N-Acetyl-Cysteine |
| Essential Oils |
| Echinacae *(Echinacae spp)* |
| Elderberry *(Sambucus nigra)* |
| Sea Buckthorn *(Hippophae rhamnoides)* |
| Ivy Leaf *(Hedra helix)* |

**TABLE 2: pre-COVID Testing Recommendations**

| CATEGORY | LABORATORY TESTING |
|---|---|
| Diabetes | Fasting glucose<br>HbA1c |
| Cardiovascular Disease | Cholesterol, lipoprotein A/B ratio, creatine kinase (CK or CK-MB), hs-CRP, blood gases, electrolytes, proBNP, Vitamin K |
| Inflammation | CRP, ESR, Ferritin, Neutrophil/ Lymphocyte ratio |
| Immune Status | CBC, Vitamin D, Omega 3 Index, Zinc, Vitamin B12, Magnesium |
| Organ Health | eGFR, Creatinine, AST, ALT |

**TABLE 3: post-COVID Testing Recommendations**

| CATEGORY | LABORATORY TESTING |
|---|---|
| CBC | Looking for progressive lymphocytopenia, leukopenia (chronically WBC may go high), eosinopenia. |
| ↑ BUN / Creatinine | Decrease in kidney function is common |
| ↑ AST, ALT, LDH | Indicates liver damage. AST/ALT ratio <1 indicates liver disease. ↑ LDH high risk indicator |
| ↑ hs-CRP, ↑ ferritin and ↑ IL-6 and other IL markers | Indicators of inflammation. |
| ↑ D-Dimer, ↑ Troponin, ↑ Cardiac myoglobin (CK-MB), ↑ proBNP | Indicate heart disease and increased risk of myocardial infarct or stroke |
| ↑ Lactic acid (l-lactate) | Indicate hypoxia |
| ↑ bicarbonate | Indicates acid-base imbalance and underventilation of the lungs. |

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## About the Authors

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