

Glutathione Deficiency May Be Associated With COVID Severity

Analysis by Dr. Joseph Mercola

✓ Fact Checked

STORY AT-A-GLANCE

- > A glutathione deficiency may be at the root of severe illness, as it leads to significant oxidative stress, lung inflammation and multiorgan failure with COVID
- > One scientist linked glutathione deficiency with many of the comorbid conditions that raise COVID-19 severity, including age, diabetes, gender and smoking
- > The researcher also found data indicating that glutathione deficiency can impact your ability to synthesize vitamin D, another risk factor for severe disease
- > NAC supplementation, foods rich in glutathione precursors, aerobic exercise and strength training can help support healthy levels

This article was previously published August 14, 2020, and has been updated with new information.

Coronaviruses were identified in the mid-1960s and so named for the crown-like spikes on the surface of the cell. Until the first SARS-CoV arrived in 2003, there were four common coronaviruses.¹ The CDC's list of symptoms for these viruses shows that they are the same as those of the common cold.² They include a runny nose, sore throat, headache, fever and cough.

However, from what scientists have discovered since the start of the global pandemic, the symptoms and long-term effects are far different for SARS-CoV-2. Initial symptoms include fever, cough, shortness of breath, fatigue and loss of taste or smell.³ However, unlike a natural coronavirus, the additional complications can affect the cardiovascular system, kidney, liver and lungs.⁴

One of the identified underlying dysfunctions that trigger shortness of breath and severe lung complications is hypercoagulability. In one study, patients who were admitted to Padova University Hospital in Italy for acute respiratory failure showed "markedly hypercoagulable thromboelastometry profiles." The researchers said:⁵

"In conclusion, COVID-19 patients with acute respiratory failure present a severe hypercoagulability rather than consumptive coagulopathy. Fibrin formation and polymerization may predispose to thrombosis and correlate with a worse outcome."

Clot formations throughout the body may be associated with other complications arising after the illness has resolved. It appears that the difference between people who have a mild or severe illness may be related to the body's ability to reduce the hypercoagulability and the hyperimmune response that leads to a cytokine storm.

How Glutathione Works – A 'Master Antioxidant?'

An antioxidant is a molecule that keeps other molecules from oxidizing. Glutathione is a powerful antioxidant that may play a significant role in the COVID-19 illness process. There are 20 amino acids that can bind together in different formations to create a protein molecule.⁶

However, glutathione is a tripeptide, which means there are only three amino acids that line up to form a glutathione molecule. These are cystine, glycine and glutamate. Together they help use and recycle other antioxidants, such as vitamin C and CoQ10.^{7,8}

This means your body uses glutathione to increase the effectiveness of these antioxidants and it helps to recycle the molecules. Without glutathione, the antioxidant capacity is significantly reduced. This function may be what earned glutathione the nickname "master antioxidant."⁹

N-acetylcysteine (NAC) plays a role as a precursor to glutathione.¹⁰ Clinical evidence has also demonstrated the effects NAC has, independent of its role with glutathione, including a thrombolytic effect. It also improves oxidative stress and the inflammatory response.^{11,12,13,14}

In late March 2020, one medical student put this theory to the test when his mother, 48-year-old Josephine Bruzzese, was diagnosed with pneumonia at NYU Langone Hospital-Brooklyn. Without an available COVID-19 test, they sent her home as a suspected case. She was prescribed hydroxychloroquine and azithromycin, which helped improve some symptoms, but not her breathing.

When she was unable to stand, and had severe respiratory problems,¹⁵ her son contacted Dr. Richard Horowitz, a specialist who was treating his sister for Lyme disease, who suggested using glutathione to help reduce the inflammation and protect Bruzzese's lung tissue. The results were dramatic.

Within one hour after receiving a 2,000 mg dose of glutathione, her breathing was better, and she could stand. She continued to take glutathione for five days and has not had a relapse. Speaking to a reporter from the New York Post, Horowitz shared that he is working to design an extensive clinical trial to prove the effectiveness of what he calls "an easy treatment that is not expensive."

May 5, 2020, Memorial Sloan Kettering Cancer Center posted a trial to [Clinicaltrials.gov](https://clinicaltrials.gov) announcing a study involving the use of NAC in patients with COVID-19. In this first-of-its-kind research, the study team plans to enroll patients with severe disease: One group in the study will receive 6 grams of NAC intravenously each day in addition to other treatments.¹⁶

Scientists Propose Deficiency Is Linked to Severe COVID-19

About the same time the study was announced by Memorial Sloan Kettering, a Russian scientist published papers proposing that glutathione plays a crucial role in a person's ability to respond to a COVID-19 infection and the resulting severity of disease.^{17,18,19} In this short video, Dr. Roger Seheult explains the science.

Additionally, Dr. Alexey Polonikov, from Kursk State Medical University, theorizes glutathione can be used as a preventive against, and treatment of, the illness. Polonikov studies human molecular genetics and oxidative stress.²⁰

Based on the exhaustive literature analysis he conducted, he later said he believes glutathione deficiency is a plausible reason for serious illness with COVID-19:²¹

"(1) oxidative stress contributes to hyper-inflammation of the lung leading to adverse disease outcomes such as acute respiratory distress syndrome, multiorgan failure and death;

(2) poor antioxidant defense due to endogenous glutathione deficiency as a result of decreased biosynthesis and/or increased depletion of GSH is the most probable cause of increased oxidative damage of the lung, regardless which of the factors aging, chronic disease comorbidity, smoking or some others were responsible for this deficit."

As Polonikov writes²² and Seheult describes in the video, oxidative damage from reactive oxygen species (ROS) plays a significant role in severe disease with COVID-19. In another video, Seheult explains how COVID-19 sets the stage for significantly increasing oxidative stress by increasing superoxide, a damaging ROS.²³

Importantly, this raises superoxide in people who start with high levels due to chronic diseases such as heart disease, diabetes and high blood pressure. As the virus uses the ACE2 enzyme, it generates angiotensin II, which in turn generates more superoxide.

The virus also attracts a type of neutrophil (polymorphonuclear leukocytes) that can also raise the production of superoxide. The superoxide then produces other hydroxyl radicals, including hydrogen peroxide (H₂O₂).

These ROSs, which cause cellular damage, can be reduced with glutathione peroxidase as it oxidizes glutathione in the process of reducing H₂O₂ to water. As you can see, a deficiency of glutathione would create a build-up for ROS as Polonikov describes.

Comorbid Risk Factors Linked to Glutathione Deficiency

Antioxidant defense against ROS damage is crucial for whole body homeostasis. Polonikov believes a higher rate of severe illness from the virus in older adults and those with comorbidities suggests there are related biological processes that make these specific individuals more sensitive. He writes:²⁴

"Specifically, impaired redox homeostasis and associated oxidative stress appear to be important biological processes that may account for increased individual susceptibility to diverse environmental insults."

In one evaluation of COVID-19 patients from six hospitals in Atlanta, researchers found independent factors that raised the risk of hospitalization. These included smoking, having Type 2 diabetes, being male, being Black, being of advanced age and being obese.²⁵ Polonikov found evidence that a glutathione deficiency may be implicated in these comorbidities.

In his paper he identifies the progressive reduction in endogenous glutathione with aging. This, he believes, makes "the elderly more susceptible to oxidative damage caused by different environmental factors compared to younger individuals."²⁶ He points out that deficiencies in endogenous glutathione are also found in people who have other comorbid conditions.

He proposes these decreased levels with chronic disease could begin a shift toward oxidative stress and exacerbate pulmonary inflammation, ultimately leading "to acute respiratory distress syndrome (ARDS), multiorgan failure and death."²⁷ Some men and some smokers also have lower levels of glutathione, which increases their risk.

In another ongoing study on the genetics of redox homeostasis and Type 2 diabetes, four patients from the control group contracted COVID-19. Blood samples were collected and used to measure ROS and glutathione levels.²⁸

All four were female nonsmokers without chronic disease who had a confirmed positive PCR test. In cases of individuals who recovered quickly, the ROS-to-glutathione ratio was 2.075-to-0.712 or less.

In patients with more significant disease, the ratio was 3.677-to-0.531 in one patient and as high as 2.73-to-0.079 in the second. In the first patient with significant disease the ratio was more than double that in patients who recovered quickly. In the second patient the ratio was more than 11 times greater.

Glutathione and Vitamin D Relationship

In terms of vitamin D, Polonikov proposes the relationship between vitamin D and severe disease may have more to do with a glutathione deficiency. He points to several studies that correlate glutathione levels with vitamin D^{29,30} and another in which scientists found that lower levels of l-cysteine, a glutathione precursor, correlated with lower vitamin D levels in people with Type 2 diabetes.³¹

In a recent animal study researchers also looked at whether glutathione deficiency could induce changes that impaired the metabolism of vitamin D.³² They found the deficiency could alter the biosynthesis and explained the mechanism for vitamin D deficiency that occurs with a glutathione deficiency.

The researchers suggest there's a potential benefit to supplementing with glutathione

in order to reduce vitamin D deficiency. Polonikov writes that this study supplies information on the importance glutathione plays in the control of endogenous vitamin D biosynthesis and demonstrates the benefits of treatment in reducing vitamin D deficiency.

I believe both nutrients are vital for protection against severe disease. While a glutathione deficiency may impact your ability to synthesize vitamin D, this is applicable only when you have enough sun exposure or supplements to raise your vitamin D level.

However, we know it is difficult to get enough sun in the Northern Hemisphere, especially during the winter months. Additionally, most people use copious amounts of sunscreen or avoid the sun altogether, which can make the deficiency problem worse.

Strategies to Support Optimal Glutathione Levels

Your glutathione levels can be optimized using food, supplements and exercise. Polonikov believes that NAC taken orally may be a preventive strategy to help support your levels. In his paper he concluded:³³

"Therefore, oral administration of N-acetylcysteine as a preventive measure against viral infections, as well as intravenous injection of NAC or reduced glutathione (GSH is highly bioavailable) in patients with serious illness may be effective options against novel coronavirus SARS-CoV-2 infection."

As he discusses in the video, Seheult believes there is more to the damage by COVID-19 than oxidative stress.³⁴ He points out that the clots removed from patients with confirmed COVID are rich with platelets, indicating another mechanism involving disulfide bonds. He goes on to explain:³⁵

"And, as we've already talked about N-acetylcysteine and reduced glutathione

will break these disulfide bonds and cause them to lyse and potentially relieve the obstruction and the hypoxemia with COVID-19. Again, this is all a hypothesis, but it looks as though it's fitting together."

Foods that have had a positive impact on glutathione production include cruciferous vegetables such as broccoli, green tea, curcumin, rosemary and milk thistle.³⁶ Getting quality sleep may also help.^{37,38}

Different types of exercise can influence your levels. In one study researchers enrolled 80 healthy but sedentary volunteers to measure the type of exercise that may have the greatest effect.³⁹ They found that aerobic training in combination with circuit weight training showed the greatest benefit.