LONG COVID March 24, 2025

In the New England Journal of Medicine, an article was published Long Covid Defined, authored by Ely, Brown, and Fineberg et.al; July 31, 2024. They describe how the COVID-19 pandemic was a dangerous acute outbreak of infection that killed more than one million people in the United States and seven million worldwide. However, more importantly, they emphasized that after the pandemic, there were many millions of people who were left with many chronic disabling symptoms which are termed "Long Covid". There have been various estimations of the incidences of long Covid as high as 10% of adults with the virus and 2% with the vaccine have been quoted. The New England article states that a survey lists numbers of 7% of adults and more than 1% of children, and this can number up to 50 to 20 million and 60 million globally with this long Covid syndrome.

A long Covid definition by a committee was formulated in this article and put forth. Cognitive impairment and neuromuscular problems, depression, and severe fatigue were hallmarks of the syndromes.

The committee did not find a standardized guideline for a developing disease definition. They used a multiphase process of systemic engagement and information gathering and included focus groups, questionaries and so forth.

The committee stated that long Covid is an infection-associated chronic condition that occurs after the SARS-CoV-2 infection and is present for at least three months as a continuous, relapsing, and remitting or progressive disease state that affects one or more organs. They go on to say that it can affect the individual in multiple ways. Shortness of breath, cough, and persistent fatigue, along with post-exertional malaise, difficulty concentrating, memory changes, recurring headaches and lightheadedness, fast heart rate, sleep disturbance, problems with taste and smell, bloating, constipation, and diarrhea are common symptoms. These are symptoms that we see very commonly in people with dysautonomia or autonomic dysregulation syndromes, that is, abnormalities of the autonomic nervous system involving either or both branches, the parasympathetic and sympathetic systems. Other viruses are known to cause these

symptoms, including Epstein-Barr, enteroviruses, and so forth. The symptoms are not specific for Covid in a post-viral syndrome.

However, the committee went on to state that singular multiple conditions, such as interstitial lung disease, low oxygen levels or hypoxemia, heart disease and arrhythmias, strokes and blood clots, kidney disease and racing heart rate when standing (postural orthostatic tachycardia syndrome), and other forms of dysautonomia and chronic fatigue-type syndromes can be present. They discussed fibromyalgia, connective tissue disease disorders, hyperlipidemia, diabetes, and autoimmune disorders, such as lupus, rheumatoid arthritis, and Sjögren's disease. They even discussed mast cell activation syndrome as being operative in a long Covid syndrome.

The committee stresses that asymptomatic infections or mild infections can also produce this long Covid syndrome and is not necessarily related to the severity of the initial Covid, or even a recurrent Covid infection. It may have a delayed onset for weeks or months and can affect children and adults.

The committee also emphasized that there are no biomarkers available to conclusively diagnose this condition. Therefore, it is purely a clinical diagnosis, and the definition is based on clinical observations and findings. There is no blood test available. They emphasize that it can cause disability and affect a person's ability to work, attend school, care for their family, and care for themselves. This is extremely important as it causes loss of work days, work productivity, and quality of life to the individuals affected. Many patients have described long Covid as having "taken their lives away from them".

As we look at the features of Long Covid Syndrome, we note that many of them are found, even without Covid infections, in individuals who have connective tissue disorders, such as Ehlers-Danlos syndrome with postural orthostatic tachycardia, mast cell abnormalities with hives, flushing, and GI-disabling symptoms, and other dysautonomia states. Chronic fatigue we feel is a manifestation of an autonomic dysfunction state where one does not get adequate blood supply to the brain and gets brain fog and cognitive dysfunction associated with it. We have previously commented

on measuring the autonomic nervous system, both the sympathetic and parasympathetic branches and observing a sympathetic withdrawal state, which causes

venous pooling, as being a major contributor to chronic fatigue both in long Covid syndrome and in dysautonomia states in general, many of which are precipitated or triggered by viral infections. Therefore, although there are no biomarkers or blood tests that can diagnose long Covid syndrome, we feel that the clinical symptoms and presentation in the proper setting, along with an objective testing of the autonomic nervous system, which looks at heart variability often coupled with respiration rate.

A terminology, which is quite technical and fancy, such as postacute sequelae of Covid (PASC), has been proposed by others, but as the authors of the New England Journal paper state, it adds nothing to the meaning, and we completely agree with this. They go on to state, as we have mentioned earlier in this communication, that there is a family of such conditions that Long Covid has in common with other viruses, bacteria and parasites and can do and that long Covid is the most recent example of this.

Is the long Covid syndrome just a unique syndrome, or is it just another example of a post-viral or post-infectious chronic fatigue state or dysautonomia state? Further study is needed in this area, and we have published a series of 152 such patients with long Covid and autonomic dysfunction. And while we have not compared other viral syndrome states with the long Covid states in terms of the incidences of dysautonomia and types and symptoms, it appears that they are oftentimes very similar in presentation, treatment and response (personal observation).

To be pure about long Covid syndrome, symptoms must be present for at least three months to fulfill the definition. This is because there could be prolonged recovery from a Covid infection as it is very inflammatory, and this may take several months as residual symptoms still linger. This three-month period can begin after an interval of what appeared to be a full recovery even after the acute infection. It is interesting that patients who have long Covid syndrome have a higher incidence of developing rheumatoid arthritis, Sjögren syndrome, systemic lupus erythematosus, or inflammatory bowel disease and diabetes than controls after they have contracted COVID-19 with higher adjusted hazard ratios.

Not everyone is at risk of long Covid, although anyone can get it. People at higher risk, according to the committee, were female sex, repeated infections, and more severe infections.

Alarmingly, it is estimated that from death certificates through 2023, The Centers for Disease Control and Prevention estimated that approximately 5000 patients in the United States have died from long Covid or from a condition in which long Covid was a contributing cause. This number is probably much higher, in our opinion.

In summary, the committee gives a very general definition of long Covid, stating that it occurs three months as a continuous relapsing and remitting or progressive disease that affects one or more organ symptoms after a SARS-CoV-2 infection. It can manifest in many ways, including singular or multiple symptoms that were described above. To repeat, shortness of breath, cough, persistent fatigue, post-exertional malaise, difficulty concentration, memory change, recurring headache, lightheadedness, a fast heart rate, sleep disturbance, problems with taste or smell, bloating, constipation, and diarrhea, are the possible manifestations of Long Covid Syndrome. Singular or multiple diagnosed conditions may result consisting of interstitial lung disease with low oxygen or hypoxemia, cardiac arrhythmia, such as atrial fibrillation, cognitive impairment that does not improve, mood disorders, anxiety, migraine, stroke, blood clots, chronic kidney disease, postural orthostatic tachycardia syndrome (POTS) and other forms of dysautonomia, chronic fatigue syndrome, mast cell syndromes, fibromyalgia, connective tissue disorders, hyperlipidemia, diabetes, and autonomic immune disease, such as lupus, rheumatoid arthritis, and Sjögren syndrome.

There have also been articles of increased incidences of ANA in people with long Covid syndrome, especially females. We have not seen this in our testing of our patients. We have not identified any autoimmune marker that is unique or specific for patients with Long Covid Syndrome. However, we do agree with the symptom complex that the committee has set forth in the three-month cutoff that they have made. We are not sure that Long Covid is much different than any long viral or long post-bacterial infection sequelae syndrome, in that they all involved autonomic nervous system dysregulation.

This comes to the most important point – treatment. Patients at times are completely disabled. We feel that attempting to test the autonomic nervous system abnormalities and treating them pharmacologically offers the best chance of symptom improvement and functional improvement. This is a slow fix and may take six months to one year to start seeing improvements. We have used vasoactive agents, volume-expanding agents, and rate-lowering agents, such as beta-blockers or Corlanor, and other agents depending on the abnormal physical findings, vital sign findings, especially with provocations, such as tilt and stand and HRV (heart rate variability) data along with pseudomotor dating. Lifestyle changes, volume expansion orally or intravenously, and antioxidant mitochondrial cocktails are also helpful in our empiric assessments.

There are several Long Covid centers that sprung up. The majority of these have closed, and when individuals look on the internet and call for appointments, they find out that a lot of them are now closed and not operating. The ones that are operating will often see patients with Telemed and will not bring them in, nor will they test their autonomic nervous system function. We feel that to get a proper evaluation, you need your autonomic nervous system evaluated and a treatment algorithm has to be put out aggressively as patients, many of them who are young, do indeed feel as though they are having their life taken from them by these post-viral syndromes and the sooner one could feel better symptomatically and have a better understanding of the disorder and can function better, the sooner their quality of life can improve, and they can get on track. There is no guarantee of successful treatment, but we have seen that along with other post-viral chronic fatigue states and autonomic dysfunction states, these treatment protocols are extremely effective in improving quality of life and function in many of our patients with these disorders, including the Long Covid Syndrome.

The following references are a study that we have published in the Journal of Neuroscience and a review article and a peer-reviewed cardiology journal to which the interested reader can refer to for more detail.