Which Long-COVID Treatment Is Right For You?

COVID-19 infection statistics are on the decline and the WHO president expects to officially declare the end of its pandemic classification in 2023. But, make no mistake, COVID-19 is still around and long COVID symptoms are still sidelining people. A July 2022 study published by the CDC showed that <u>1 in 5</u> Americans who had COVID still have Long COVID symptoms.

Most lingering symptoms are signs of either inflammation in the brain, lack of blood flow, immune dysregulation, sympathetic nervous system dysfunction, or cellular dysfunction. Common symptoms include:

Fatigue Dizziness Difficulty concentrating Headaches Shortness of breath Anxiety And more

Just as acute COVID-19 infections impact people differently, Long COVID symptoms don't always manifest equally. As doctors continue to research the short and long-term implications of COVID infections, more treatment possibilities for lingering symptoms are emerging.

Here at Hudson Health we offer a wide range of Long COVID treatments that correspond to specific symptoms and Long COVID-induced system dysfunctions.

Based on our experience, we have had success with treatments that address some of the root systematic dysfunctions at the cellular level. Some of these treatments include peptide therapy, nerve blocks of the sympathetic system, IV therapies, and ozone dialysis

We have concluded our first IRB-approved study: "<u>The use of Dual-Sympathetic Blocks in treating</u> <u>dysautonomia in Long-Covid</u>" which will be published soon.

Read on to learn about the treatments that may help your Long COVID symptoms.

Autonomic Nervous Dysfunction

Long COVID is known for wreaking havoc on the Autonomic Nervous System (ANS), which is responsible for maintaining involuntary body functions like heart rate, blood pressure, digestion, and breathing (1). The ANS consists of two parts: the sympathetic nervous system (SNS), which regulates the fight-or-flight response and the parasympathetic nervous system (PNS), which regulates the rest-and-digest response.

Researchers are still defining the exact mechanisms by which Long COVID causes Autonomic Nervous Dysfunction. Some theories suggest that the immune response triggered by the initial infection may result in inflammation and damage to the nervous system, including the autonomic nervous system. This initial inflammatory response has been shown to cause microvascular injuries to the blood-brain barrier (BBB), a highly dense network of cells that are responsible for keeping harmful substances like viruses or other pathogens from reaching the brain. When the BBB becomes altered or weakened, it becomes increasingly difficult for the ANS to regulate the cerebral blood flow response, a process that regulates blood flow to and throughout the brain. Impaired cerebral blood flow response may lead to an overdrive of the sympathetic nervous system (2). This hyperactive state is a compensatory mechanism, and if it is not effectively and efficiently addressed, it can result in blunted baroreceptor responsiveness. Baroreceptors act as a feedback system to the cardiovascular system-controlling centers of that brain, and when appropriately activated, they reduce sympathetic signaling. In diseases that cause a hyperactive sympathetic state such as Long COVID, sympathetic overdrive over stimulates these baroreceptors, leading to decreased sensitivity and functioning (3,4). The body responds by either significantly increasing heart rate or increasing diastolic blood pressure to ensure that the brain is receiving sufficient blood flow (5). In addition, it is believed that the virus may directly invade and damage nerve cells, leading to dysfunction in various parts of the body, including the autonomic nervous system.

In healthy individuals, autonomic nervous system nerve fibers control our blood pressure through a mechanism called the vasomotor response, which determines our blood pressure by carefully regulating whether or not small blood vessels and capillaries are constricted or dilated at any given moment. In Long COVID, a phenomenon known as vasomotor denervation causes prolonged and inappropriate dilation of these blood vessels (6). Dilated blood vessels caused by vasomotor denervation can lead to reduced preload to the heart, which triggers an increase in sympathetic signaling. In essence, in Long COVID, autonomic nervous dysfunction can significantly impair our ability to shunting blood to the areas of the body where it is needed (7). In turn, patients with Long COVID may experience symptoms like dizziness, chronic fatigue, palpitations, shortness of breath (8).

Long COVID patients also may experience symptoms related to temperature dysregulation. Research suggests that these symptoms may be attributed to hypothalamic dysfunction as a result of autonomic dysfunction (9). The hypothalamus is a brain structure that works like a thermostat, keeping the body temperature appropriate in the context of the environment and the immune system. The BBB in and around the hypothalamus is highly permeable to blood-borne substances, including viruses. Studies have found increased viral load in the hypothalamic region of the brain, indicating that the virus uses this area to access brain cells (10). As the hypothalamus is involved in thermoregulation, COVID infection may cause a dysregulation of body temperature.

Signs of Autonomic Nervous System Dysfunction

Heart palpitations or racing heartbeat Fluctuations in blood pressure Dizziness or lightheadedness upon standing

Sweating or changes in body temperature regulation

Fatigue or weakness Shortness of breath or difficulty breathing Cognitive symptoms such as brain fog, memory problems, or difficulty concentrating Insomnia or changes in sleep patterns.

Treatment Option: Dual Sympathetic Block

Dual Sympathetic Block

If any of the above symptoms resonate with you, a Dual Sympathetic Block (DSB) can restore balance to your overly-heightened nervous system. These blocks are injected in the neck, along the sympathetic chain and in the Stellate Ganglion nerve cluster, which influences your sympathetic response. By temporarily anesthetizing the nerve clusters, DSBs give the system a chance to reset to a more neutral biological level.

Having performed thousands of Dual Sympathetic Blocks, Hudson Medical is considered a global leader in DSB administration and an industry leader in Dual Sympathetic Block clinical research.

Explore Hudson Medical's DSB Research: Botox-Enhanced Stellate Ganglion Blockade for the Treatment of Post-Traumatic Stress Disorder Stellate Ganglion Block for Long COVID Stellate Ganglion Block for Anxiety Stellate Ganglion Block – The Science

Neurological Dysfunction

One of the most common systems impacted by daily Long COVID symptoms is the neurological system. A 2022 JAMA network study demonstrated <u>brain fog as one of the most commonly-reported Long</u> <u>COVID symptoms</u> (11).

Like other symptoms of COVID-induced dysregulation, the exact mechanisms that induce ongoing brain fog remain ill-defined. However, it is widely believed that inflammation from acute COVID infection may be linked to a decrease in cognitive functioning. When inflammation occurs in the brain in response to infection, it can lead to the release of inflammatory molecules like cytokines that can disrupt the normal functioning of brain cells and neural circuits. This disruption can interfere with the communication between neurons and affect the way that different brain regions work together, leading to neurological symptoms such as difficulty concentrating, headaches, and brain fog.

Migraines are also a common symptom of Long COVID. In the context of Long COVID, migraines may be due to an increase in intracranial pressure (IP), the pressure exerted by fluids inside the skull and on the brain tissue. Increased IP may be a result of faulty autonomic nervous system regulation of cerebral

blood flow (the blood flow to and throughout the brain). This increased IP is sensed as pain anywhere on the cranium, but especially around the frontal lobes (12).

Tinnitus is a ringing or buzzing noise in one or both ears that may be constant. Tinnitus can occur on occasion or chronically with Long COVID dysautonomia. Tinnitus may occur as a result of decreased blood flow and hyperinflammation of the Cranial Nerve that controls functions of the ear (13).

Additionally, sleep problems have been identified in Long COVID and can occur occasionally or chronically. The autonomic nervous system controls the sleep cycle and the deep sleep cycle and REM sleep can be affected when the autonomic nervous system is dysregulated.

Signs of Neurological Dysfunction

Difficulty concentrating Consistent headaches Migraines Tinnitus Sleep Irregularity

Potential Treatment(s) for you: NAD+ Infusion Therapy, Methylene Blue, Ketamine IV, Peptides, Prescription Medications

NAD+ Infusion Therapy

Nicotinamide adenine dinucleotide, NAD+, is a coenzyme that influences some of the most vital processes in the body, including how food is metabolized into energy, DNA repair, and overall immune system functioning.

Studies have shown that viral infections like COVID-19 may deplete NAD+ stores. NAD+ infusions can boost mitochondrial function, improve prolonged fatigue and neurocognitive dysfunction, and may suppress post-COVID inflammation.

Ketamine IV Therapy

Low-dose ketamine infusions may significantly reduce symptoms of anxiety and depression. Research shows that lasting anxiety and depression can actually change the composition of the brain and damage some neural connectivity. Ketamine restores dormant neural circuits by triggering the production of Glutamate, which in turn, promotes BDNF, a protein that encourages neuroplasticity in the brain. Ketamine has also been shown to influence the activity of other neurotransmitter systems that are involved in the regulation of mood, including dopamine (14).

Methylene Blue

Methylene Blue is a compound that may aid the transportation of oxygen throughout the body by targeting mitochondrial dysfunction. Emerging research suggests that Methylene Blue may have

neuroprotective effects, including: mitigating oxidative stress, increasing blood flow to the brain, and reducing inflammation and cellular death. Methylene blue can be given either via IV infusion or orally.

Peptide Therapy

Peptides are short chains of amino acids that influence major biological processes. Peptide therapy reinforces our natural supply to help regulate and promote these biological processes. BPC and TB4 are two peptides known for their anti-inflammatory and immunomodulating effects. **Selank** and **Semax** are two peptides known for their nootropic and neuroprotective effects. Selank improves anxiety and mood, while Semax improves attention and concentration. **KPV** is a powerful anti-inflammatory peptide that is administered via intranasal spray.

Medications

Guanfacine and NAC

Guanfacine is a prescribed oral medication that works by stimulating certain receptors in the brain and reducing the activity of the sympathetic nervous system, which helps to lower blood pressure and improve ADHD symptoms.

NAC is derived from amino acids and known for its antioxidant properties. It may be prescribed as an oral medication or administered intravenously. Guanfacine and NAC may be prescribed in tandem to combat COVID-related brain fog (15).

Immune Dysregulation

Immune dysregulation following a COVID diagnosis is characterized by both hyperinflammatory and immunosuppressive conditions (16). Our immune systems are responsible for automatically responding to the threat of infection, and when this system is disrupted, the body does not appropriately respond to threats–resulting in either underreaction or overreaction. Research has demonstrated that the COVID virus has the ability to evade some of the immune system's antiviral defenses, which can cause a delayed but magnified inflammatory response and is responsible for the characteristic mild initial stage of COVID infection (17). A postponed but enhanced inflammatory immune response leads to significant tissue damage and rapid progression of the infection through the excessive production of pro-inflammatory molecules like cytokines (18). Further, recent research has demonstrated that patients with Long COVID have highly activated immune cells that remain persistently activated for over 8 months after infection. In essence, the immune response becomes dysregulated during active COVID infection and, for those with Long COVID, remains dysfunctional for some time (19). Additionally, in response to COVID infection, the body may produce a variety of autoantibodies, including functionally active autoantibodies against G-protein-coupled receptors (GPCR-AAbs) (20). Some of these autoantibodies are associated with impaired circulation and neurological dysfunction.

Signs of Immune Dysregulation

Widespread joint pain Night sweats Skin rashes Change in appetite Low blood pressure Headaches Fatigue

Treatment options: Peptide therapy, IV Infusions,Ozone Dialysis EBOO, Medication (Oral and Infusions), Histamine Blockers,

Peptide Therapy

Thymosin Beta 4 reduces inflammation and promotes regeneration while Thymosin Alpha 1 can improve your immunity and bolster your body's defenses against infections.

IV Infusions

To combat immune dysregulation, IV infusions may include NAD, peptide immunomodulators, glutathione, NAC, and various additional vitamins to boost your body's immune system and energy.

Ozone Dialysis EBOO

Extracorporeal Blood Oxygenation and Ozonation (EBOO) is a form of ozone therapy known for its efficacy in combating inflammatory conditions and autoimmune disorders. An EBOO procedure uses dialysis filters to essentially clean out germs and toxins from a patient's bloodstream. Blood is drawn from a patient's vein, and ozonated in a contained and sterile chamber before being reintroduced into the bloodstream via a separate vein.

Oral Medication

Low-dose Naltrexone is known for its immune-modulating effects and is helpful in both treating and preventing immune issues (21). Low-dose Naltrexone for immune dysfunction is considered an off-label treatment.

Lithium Orotate is known for its anti-inflammatory properties. Clinical studies have found significant improvement in patients taking lithium for Long COVID symptoms like fatigue and brain fog (22).

Histamine Blockers

Researchers are studying the link between Long Covid and Mast Cell Activation, a process in which mast cells (a type of immune cell that defends against pathogens and allergens) are activated and release histamines and inflammatory mediators (23).

Histamine H1 and H2 blockers (like claritin and famotidine, respectively) are effective against common symptoms related to histamine release, like itching, swelling and respiratory distress.

Cardiopulmonary Dysregulation

Shortness of breath is one of the most notable symptoms of acute COVID infection, and long COVID sufferers also commonly experience persistent breathing complications. Breathing is an involuntary mechanism controlled by the autonomic nervous system, which regulates the opening and closing of air passages (24). When the autonomic nervous system is impacted from COVID-induced inflammation, air passages are hindered and patients often report feeling as though they are only able to inhale a fraction of their typical breath capacity.

Signs of cardiopulmonary dysregulation

Shortness of breath Dizziness Chest pain Fainting

Treatment options: Dual Sympathetic Block

Our airways are innervated by autonomic nerve fibers, so autonomic dysfunction may lead to problems regulating the activity of our airways. A Dual Sympathetic Blocks temporarily anesthetizes a cluster of nerves in the neck that influence the nervous system. Following this brief timeout, the system is able to reset at a more normal level which can restore autonomic functioning.

Mitochondrial Dysfunction

Many Long-COVID patients report increased difficulty in performing their regular pre-COVID exercise routines. Although there are likely many disrupted physiological processes that contribute to this phenomenon, mitochondrial dysfunction may play a key role. Your mitochondria are small structures found in most cells that are responsible for producing energy. Mitochondria play a critical role in providing energy to the body's cells, and any dysfunction in these structures can have a significant impact on overall cellular and bodily function.

Signs of Mitochondrial Dysfunction

Fatigue Muscle weakness Imbalance Lack of coordination

Treatment options: NAD+ Infusion, Peptide Therapy, Hyperbaric Oxygen Therapy, Medication

NAD+ Infusion

Nicotinamide adenine dinucleotide, NAD+, is a coenzyme that influences some of the most vital processes in the body, including how food is metabolized into energy, DNA repair, and overall immune system functioning. Studies have shown that viral infections like COVID-19 may deplete NAD+ stores (25). NAD+ infusions can boost mitochondrial function, improve prolonged fatigue and neurocognitive dysfunction, and may suppress post-COVID inflammation.

Peptide Therapy

Humanin, SS-31 and MOTSc are all known for their ability to boost mitochondrial function. **MOTSc** is considered a mitochondrial-derived peptide made up of 16 amino acids. Research has found that MOTSc influences metabolic function, inflammation and insulin resistance (26).

Humanin is a mitochondrial-derived peptide consisting of 24 amino acids. Known for enhancing insulin sensitivity and protecting against age-related metabolic disorders, Humanin has emerged as an essential longevity-boosting peptide (27).

SS-31, also known as Elamipretide, is a synthetic peptide known for stabilizing mitochondrial function. SS-31 permeates cells and decreases reactive oxygen species production and enhances overall energy production (28).

Learn more about Hudson's peptide therapy program.

Exogenous Ketone Therapy

Ketones are molecules produced by the body when it breaks down fat for energy, instead of using carbohydrates. One type of ketone called R- β HB can influence energy production by balancing NAD+ and NADH ratios in cells (29). Supplementing this type of ketone can also help to maintain functioning mitochondria by reducing oxidative stress and inflammation.

Hyperbaric Oxygen Therapy

Hyperbaric Oxygen Therapy is a treatment that involves breathing pure oxygen in a pressurized environment. This type of therapy may help mitochondrial dysfunction by increasing the availability of oxygen to cells and tissues throughout the body, including the mitochondria.

Musculoskeletal Dysfunction

Muscle weakness and spasms are also common physical responses after an acute COVID diagnosis. These symptoms are believed to be caused by reduced blood flow and energy supply to the muscles due to a malfunctioning autonomic response. In Long COVID, chronic hyperinflammation is closely associated with muscle breakdown (30). Dysfunction of the immune system after COVID can cause the excessive production of pro-inflammatory molecules with well known roles in negatively impacting the metabolism of proteins in muscle (31). Muscle pain and spasms may also result from the accumulation of lactic acid due to lack of energy.

Signs of Musculoskeletal Dysfunction Muscle Pain Muscle fatigue Numbness Muscle Spasms

Treatment options: Peptides, Regenerative Therapy, Hydrodissection, Interventional Pain Management, Physical Therapy

Peptides

BPC-157 enhances healing processes by reducing inflammation and increasing blood flow around damaged tissue.

TB4 is known for its anti-inflammatory properties and promotion of tissue repair and regeneration. **GHK-Cu** stimulates collagen, reduces oxidative damage, and generates healthy tissue.

Regenerative Therapy

Exosome Infusions harness the critical role exosomes play in intracellular communication. Derived by donor cells, exosomes promote healing and restoration of damaged tissues.

Platelet-rich plasma therapy is a type of therapy that extracts and processes highly concentrated platelets from your own blood. Once processed, the platelet concentration is injected into the injured area to promote faster healing and tissue regeneration.

Learn more about Hudson Medical's regenerative treatments.

Interventional Pain Management

Hydrodissection involves the injections of fluid under ultrasound into injured muscles in order to separate inflamed tissue. Creating a separation between injured muscle and surrounding fascia and nerves may reduce pressure and promote blood flow to the injured area.

Steroid Injections involve injecting afflicted joints or tendons with a steroid medication to reduce inflammation and alleviate pain.

Nerve Blocks involve injecting a steroid medication near a nerve that is causing pain. The medication temporarily blocks the nerve's ability to transmit pain signals, providing pain relief.

Nerve Ablations utilize heat to effectively block the brain from processing pain signals transmitted by nerves in the spine.

Learn more about Hudson Medical's interventional pain treatments.

Physical therapy uses a combination of stretching and strengthening exercises to improve mobility and prevent future strain. Here at Hudson we offer a specialized CAMP program that administers physical therapy with targeted acupuncture, medical massage, and chiropractic care. These successive treatments alleviate discomfort while restoring whole-body balance.

Psychological Dysfunction

It's not just the stress of recovering from sickness, many people who are diagnosed with an acute COVID infection report lingering feelings of increased anxiety and depression. In fact, some studies report that Long COVID is associated with an estimated 13% increased presence of depression, 28% increase in anxiety, 10% increase in suicide ideation, and 20% increase in PTSD compared to healthy individuals (32). Further, these emotional and psychological disorders can lead to decreased life satisfaction and daily functioning. Studies have found that inflammation from the virus may actually spark changes in the brain's composition. Research has also demonstrated that psychological distress is not only a symptom but also a risk factor of long COVID (33).

Signs of Psychological Dysfunction

Persistent sadness Irritability Insomnia Difficulty Concentrating

Treatment options: Interventional Mental Health Treatments

Hudson Mind, Hudson Health's interventional mental health division, offers a range of interventions proven to combat the physical and emotional symptoms of anxiety and depression.

TMS

Transcranial magnetic stimulation (TMS) is a noninvasive brain stimulation therapy used to treat psychiatric disorders like depression, migraines, and obsessive compulsive disorder (34,35). In order to understand how TMS can provide significant and lasting depression symptom relief, it is essential to discuss how brain function is altered in patients with depression. TMS involves the application of targeted magnetic pulses to the superficial layers of the brain. This magnetic field is able to induce small electrical currents that stimulate nerve cells in mood-controlling areas of the brain (36, 37, 38, 39, 40). These small electrical currents are powerful enough and precise enough to elicit an activating signal in brain cells to release more neurotransmitters and therefore can increase the activity of connecting neurons. TMS is able to address the neurotransmitter imbalance associated with depression by stimulating targeted neurotransmitter release in mood-controlling areas of the brain (37).

IV Ketamine

Low-dose ketamine infusions may significantly reduce symptoms of anxiety and depression. Research shows that lasting anxiety and depression can actually change the composition of the brain and damage some neural connectivity. Ketamine restores dormant neural circuits by triggering the production of Glutamate, which in turn, promotes BDNF, a protein that encourages neuroplasticity in the brain. Ketamine has also been shown to influence the activity of other neurotransmitter systems that are involved in the regulation of mood, including dopamine.

Dual Sympathetic Blocks

A minimally-invasive anesthetic that alleviates symptoms of PTSD. By temporarily anesthetizing the nerve clusters, DSBs give the sympathetic nervous system a chance to reset to a more neutral biological level. Also known as Stellate Ganglion Block (SGB).

Don't know which treatment is best for your symptoms? Our team is here to help you navigate our Long COVID offerings. <u>Schedule your Long COVID Consultation</u>

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