

# I-RECOVER<sup>SM</sup>

## LONG COVID TREATMENT

### An Approach to Treating Long COVID

Long COVID, a prolonged illness after COVID-19, may persist for months after the acute infection and affects at least 65 million individuals worldwide. A puzzling feature of long COVID is that initial disease severity is not an accurate predictor; long COVID frequently occurs in people who had mild-to-moderate COVID cases as well as in younger adults who did not require respiratory support or intensive care. Patients with long COVID should be managed by clinicians who have experience treating this troublesome disorder. Early treatment is essential; the response to treatment will likely be attenuated when treatment is delayed.

### WHAT IS LONG COVID?

Many patients experience prolonged illness after COVID-19. This is commonly known as 'long COVID', though it also referred to as 'Long Haul COVID Syndrome (LHCS)' or 'Post-acute sequelae of COVID-19 (PASC)'.

Long COVID may persist for months after the acute infection and almost half of patients report reduced quality of life. At least 65 million individuals worldwide are estimated to have long COVID.

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### WHAT ARE THE SYMPTOMS OF LONG COVID?

Many of the symptoms of long COVID are common to COVID-19 vaccine injury (also known as long vax); indeed, both disorders are considered manifestations of "spike protein-related disease" with a significant overlap in symptoms, pathogenesis, and treatment.

The major difference between long COVID and long vax is unresolved organizing pneumonia with persistent respiratory symptoms. Clinicians have also noted that long-vax patients tend to have more severe illness due to a higher incidence and severity of neuropathic symptoms and dysautonomia.

Long COVID and long vax are heterogeneous syndromes, meaning their symptoms and clinical features vary widely in presentation, severity, and underlying causes or contributing factors. Both are characterized by prolonged malaise, headaches, generalized fatigue, sleep difficulties, hair loss, smell disorder, decreased appetite, painful joints, dyspnea, chest pain, and cognitive dysfunction. Patients may suffer prolonged neuropsychological symptoms, including multiple domains of cognition.

The symptom set of long COVID is, in the majority of cases, very similar to chronic inflammatory response syndrome (CIRS)/myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). An important differentiating factor from CIRS is the observation that long COVID continues to improve on its own, albeit slowly in most cases. Another important observation is that long COVID includes more young people compared to severe COVID, which affects older people or persons with comorbidities. Furthermore, the similarity between mast cell activation syndrome (MCAS) and long COVID has been observed, and many consider long COVID to be a variant of MCAS.

### About this protocol

The information in this document is our recommended approach to long COVID and spike protein related disease. It based on the best (and most recent) literature and aims to provide guidance to healthcare providers worldwide.

Our guidance should only be used by medical professionals in formulating their approach to patients with COVID-19 and spike protein related disease. Patients should always consult with a provider before starting any medical treatment.

New medications may be added and/or changes made to doses of existing medications as further evidence emerges. Please check our website at [flccc.net](https://flccc.net) to be sure you are using the latest version of this protocol.

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Furthermore, due to the marked overlap between long COVID and post-vaccine syndrome, please refer also to the **I-RECOVER Post Vaccine Treatment** strategy. This document highlights the differences between the two syndromes.

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## GROUPS OF SYMPTOMS

The clinical signs and symptoms can be grouped into the following clusters. The reason for this grouping is to allow organ-specific targeted therapy or individualized therapy:

1. Respiratory: shortness of breath, congestion, persistent cough, etc.
2. Neurological/psychiatric: brain fog, malaise, tiredness, headaches, migraines, depression, inability to focus or concentrate, altered cognition, insomnia, vertigo, panic attacks, tinnitus, anosmia, phantom smells, etc.
3. Musculoskeletal: myalgias, fatigue, weakness, joint pains, inability to exercise, post-exertional malaise, inability to perform normal activities of daily life
4. Cardiovascular: Palpitations, arrhythmias, Raynaud-like syndrome, hypotension, and tachycardia on exertion
5. Autonomic: Postural tachycardia syndrome (POTS), abnormal sweating
6. Gastrointestinal disturbance: anorexia, diarrhea, bloating, vomiting, nausea, etc.
7. Dermatologic: itching, rashes, dermatographia
8. Mucus membranes: running nose, sneezing, burning and itchy eyes

## GENERAL APPROACH TO TREATMENT

Patients with long COVID should be managed by clinicians who have experience treating this troublesome disorder. The treatment approach should be individualized according to the grouping of clinical signs and symptoms.

However, in general, it is likely that patients who did not receive adequate antiviral treatment (e.g., ivermectin, etc.) and adequate anti-inflammatory/macrophage repolarization treatment during the acute symptomatic phase of COVID-19 are more likely to develop long COVID.

The core problem in long COVID is chronic “immune dysregulation.” The primary treatment goal is to help the body to restore and normalize the immune system — in other words, to let the body heal itself. We recommend the use of immune-modulating agents and interventions to dampen and normalize the immune system rather than the use of immunosuppressant drugs, which may make the condition worse. However, the concomitant use of a controlled course of an immunosuppressant drug may be appropriate in patients with specific autoimmune conditions.

In addition to treating organizing pneumonia, as noted below, our suggested treatment strategy involves two major approaches i) promote autophagy to help rid the cell of the spike protein and ii) interventions that limit the toxicity/pathogenicity of the spike protein.

Early treatment is essential; the response to treatment will likely be attenuated when treatment is delayed.

Patients should be started on the primary treatment protocol; this should, however, be individualized according to the patient’s particular clinical features. The response to the primary treatment protocol should dictate the addition or subtraction of additional therapeutic interventions. Second-line therapies should be started in those who have responded poorly to the core therapies and in patients with severe incapacitating disease.

**NOTE:** Patients with long COVID must not receive further COVID-19 vaccines of any type.

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## DIAGNOSTIC TESTS

The following basic tests are recommended — tests such as cytokines and chemokines, autoantibodies, and toxicological studies are expensive, have very little clinical relevance, and only complicate the management of long COVID patients.

- CBC with lymphocyte count and CD8+ count
- Chemistry with liver function tests
- CRP (inflammation)
- Ferritin (macrophage activation)
- D-dimer
- Early morning cortisol
- Thyroid function tests
- HbA1C—long COVID patients are at an increased risk of developing diabetes
- Autoantibodies: antiphospholipid antibody and ANA
- In patients with allergic features or those who experienced an acute reaction to the vaccine, the following tests may be helpful: eosinophil count; IgE levels, RAST testing and/or skin testing. Serum tryptase, serum histamine and/or 24-h urine N-methylhistamine should be considered in MCAS. (22)
- Reactivated viruses: Antibodies/PCR against EBV Herpes I/II and CMV
- Vitamin D level

## Specific Phenotypic tests

- CXR / chest CT with contrast
- Brain MRI
- ECHO

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## TREATING ORGANIZING PNEUMONIA

As noted previously, the major difference between long COVID and long vax is unresolved organizing pneumonia with persistent respiratory symptoms. Therefore, in patients with ongoing respiratory symptoms, chest imaging is suggested (preferably a chest CT scan).

Those with unresolved pulmonary inflammation (organizing pneumonia with ground glass opacification) should be treated with a course of corticosteroids. Low-dose prednisolone/methylprednisolone (10 mg/day) for six weeks is suggested. However, the patient's symptoms and CRP should be followed closely, as a dose escalation may be required in those who respond poorly.

An unknown number of patients who have recovered from COVID-19 organizing pneumonia will develop pulmonary fibrosis with associated limitation of activity. Pulmonary function testing demonstrates a restrictive type pattern with decreased residual volume and DLCO. These patients should be referred to a pulmonologist with expertise in pulmonary fibrosis. Anti-fibrotic therapy may have a role in these patients, however additional data is required before this therapy can be more generally recommended. The serotonin receptor blocker cyproheptadine may reduce the risk of pulmonary fibrosis.

## FIRST-LINE THERAPIES

*(Not symptom specific; listed in order of importance; see full treatment strategy for detailed dosing information)*

- **Intermittent daily fasting or periodic daily fasts:** Fasting stimulates the clearing of damaged mitochondria (mitophagy), misfolded and foreign proteins, and damaged cells (autophagy). Autophagy likely removes spike protein and misfolded proteins induced by the spike protein. Autophagy may therefore play a critical role in reversing the "spikopathy" induced by COVID infection. Indeed, activation of autophagy may be the only mechanism to remove intracellular spike protein.
- **Ivermectin:** It is likely that ivermectin and intermittent fasting act synergistically to rid the body of the spike protein. Ivermectin binds to the spike protein, aiding in the elimination by the host. Ivermectin also has potent anti-inflammatory properties.
- **Moderating physical activity:** Patients with long COVID frequently suffer from severe post-exertional fatigue and/or worsening of symptoms with exercise. We recommend moderating activity to tolerable levels that do not worsen symptoms, keeping the patient's heart rate under 110 BPM. Furthermore, patients need to identify the activity level beyond which their symptoms worsen, and then aim to stay below that level of activity. Stretching and low-level resistance exercises are preferred over aerobic exercises.
- **Low-dose naltrexone:** This medication has been demonstrated to have anti-inflammatory, analgesic, and neuromodulating properties.
- **Nattokinase:** This highly effective fibrinolytic and antiplatelet agent targets the abnormal clotting that can occur from spike protein-related disease.
- **Melatonin:** A powerful regulator of mitochondrial function, melatonin has anti-inflammatory and antioxidant properties. Should be taken prior to bedtime.
- **Magnesium:** At least 11 different types of magnesium are available, with varying bioavailability.
- **Low-dose Methylene Blue:** This is a therapeutic option in patients with brain fog and other neurological symptoms. The optimal dose is highly individualized and each patient needs to find the right dose for them.
- **Sunlight and Photobiomodulation (PBM):** Sunlight has great therapeutic powers. We suggest patients expose themselves to about 30 minutes of midday sunshine whenever possible (at least 3 times a week). A brisk midday walk is a viable alternative, as is red and NIR radiation emitted from LED panels.

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## ABOUT INTERMITTENT FASTING

Many people ask how to remove spike protein from the body.

The FLCCC recommends intermittent fasting as one of the most effective ways to induce autophagy, the process by which the body clears out damaged and misfolded cells.

We additionally suggest time-restricted feeding as a lasting lifestyle intervention to promote health, reduce disease burden, slow aging, prevent neurodegenerative disease, prevent cardiovascular disease, and prevent cancer.

**Learn more:** [Eat Well: Guide to Fasting and Healthy Eating](#)

## ABOUT IVERMECTIN

Ivermectin is a well-known, FDA-approved drug that has been used successfully around the world for more than four decades. One of the safest drugs known and is on the WHO's list of essential medicines. It won the Nobel Prize for its global and historic impacts in eradicating endemic parasitic infections in many parts of the world.

Review the **totality of supporting evidence** for ivermectin.

Ivermectin is a remarkably safe drug with minimal adverse reactions (almost all minor), however its safety in pregnancy has not been definitively established. Talk to your doctor about use in pregnancy, particularly in the first trimester.

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### FIRST-LINE THERAPIES, CONTINUED

(Not symptom specific; listed in order of importance; see full treatment strategy for detailed dosing information)

- **Vitamin D and K2**
- **Resveratrol or a combination flavonoid**
- **Probiotics/prebiotics:** Patients with long COVID classically have a severe dysbiosis with loss of Bifidobacterium.

### SECOND-LINE/ADJUNCTIVE THERAPIES

(Listed in order of importance; see full treatment strategy for detailed dosing information)

- **Omega-3 fatty acids:** We suggest a combination of EPA/DHA.
- **N-acetyl cysteine (NAC):** NAC has a broad range of antioxidant, anti-inflammatory, and immune-modulating mechanisms.
- **Cardio Miracle™ and L-arginine/L-citrulline supplements:** These supplements increase nitric oxide (NO) production.
- **Nigella sativa:** Taken as a supplement, in oil form, or as seeds, nigella sativa (also known as Black Seed or Kalonji) has antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, and immunomodulatory properties.
- **Sildenafil** with or without L-arginine-L-Citrulline: This may be helpful for brain fog as well as microvascular disease with clotting and poor perfusion.
- **Bromelain:** In vitro studies have demonstrated that bromelain cleaves the spike protein. This effect may be enhanced by NAC.
- **Vitamin C:** This vitamin is essential to human health and has important anti-inflammatory, antioxidant, and immune-enhancing properties. Oral Vitamin C also helps promote the growth of protective bacterial populations in the microbiome.
- **Spermidine:** Spermidine is a naturally occurring polyamine that, like resveratrol, has anti-inflammatory and antioxidant properties.
- **Non-invasive brain stimulation (NIBS):** Using transcranial direct current stimulation or transcranial magnetic stimulation, NIBS has been demonstrated to improve cognitive function in patients with long COVID as well as other neurological diseases.
- **Intravenous Vitamin C**
- **Behavioral modification, relaxation therapy, mindfulness therapy**

### THIRD-LINE THERAPIES

- **Hyperbaric oxygen therapy**
- **Low Magnitude Mechanical Stimulation**
- **“Mitochondrial energy optimizer”**
- **Hydroxychloroquine**
- **Low dose corticosteroid**



#### **A note about anesthesia and surgery:**

*Patients should notify their anesthesia team if using the following medications and/or nutraceuticals, as they can increase the risk of Serotonin syndrome with opioid administration:*

- Methylene blue
- Curcumin
- Nigella Sativa
- Selective Serotonin Reuptake Inhibitors (SSRIs)

### ABOUT METHYLENE BLUE

Low-dose Methylene Blue will cause your urine to be blue or blue-green. Some patients may experience a Herx reaction, which may cause fatigue, nausea, headache, or muscle pain. If you experience a Herx reaction, stop the protocol for 48 hours and then resume again slowly.

MB is a potent monoamine oxidase inhibitor that, in conjunction with an SSRI, can potentiate serotonin syndrome, a life-threatening medical emergency. This combination of medications is to be strongly avoided. **Do not take FLUVOXAMINE, FLUOXETINE or BUPROPION or any other SSRI -NDRI (norepinephrine-Dopamine Reuptake Inhibitor) with MB.**

MB increases toxicity of hydrocodone bitartrate by increasing serotonin levels in the blood. This combination should be avoided.

Individuals with glucose-6-phosphate dehydrogenase deficiency (G6PD) should not be treated with MB as it can cause hemolytic anemia.

**DO NOT take MB if you are pregnant or breastfeeding.**

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