

FREE  
CHAPTERS

EXCERPT:  
**COMPLETE  
LONG COVID  
HANDBOOK**  
VOLUME 2

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# Long Covid Risk Factors



**L**ong COVID comprises many symptoms that can vary significantly between individuals. These symptoms vary because each person with Long COVID contributes differently from the four causes. Autoimmune conditions and blood clots are consequences of the four causes rather than the causes themselves.

## Risk Factors for Getting Long COVID

Understanding who is most at risk for developing Long COVID is vital for prevention and treatment. Having one of these risk factors does not guarantee you will come down with Long COVID. This section reviews the current epidemiological data, including prevalence rates, demographic factors, and potential risk factors such as preexisting health conditions, severity of initial infection, and sociodemographic variables. All of these can potentially increase your risk of getting Long COVID, but it is not a guarantee that you will get it. Primarily, any condition that is associated with dysautonomia or autonomic neuropathy increases your risk. The bottom line is that having preexisting autonomic nervous system damage or defect is a significant risk factor for Long COVID. A risk factor is a risk, not a guarantee that you will get Long COVID. The risk for Long COVID remains even after you recover.

**Risk factors** are associated with preexisting damage to the autonomic nervous system, also known as autonomic neuropathy or dysautonomia. The conditions causing this situation are listed below:

- Preexisting herpes family viral infections such as *Cytomegalovirus* (CMV), *Ebstein-Barr Virus* (EBV), *Human Herpes Virus* (HHV-6,

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roseola infantum), HHV-7 (roseola infantum, exanthem subitem (ES), or 6<sup>th</sup> disease), chicken pox (varicella herpes zoster)

- Prior Lyme disease or other spirochete infections
- *Erlor-Danlos Syndrome* (EDS)
- Preexisting autoimmunity such as *Crohn's* disease, ulcerative colitis, rheumatoid arthritis, lupus/SLE, Sjogren's syndrome
- Preexisting *Dysautonomia – Postural Orthostatic Tachycardia Syndrome* (POTS), Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), Post Traumatic Stress Disorder (PTSD), diabetes mellitus
- Vitamin B6 toxicity

**In addition, there are some risk factors for other reasons:**

- Female >> male gender
- Age being under 50 years old
- Number of COVID-19 infections (risk for Long COVID increases by 5% each time)
- Preexisting gut dysbiosis
- Having five or more symptoms during the 1<sup>st</sup> week of an acute COVID-19 infection
- Physical or emotional stress and traumatic events

**References:**

1. Subramanian, A., Nirantharakumar, K., Hughes, S. *et al.* Symptoms and risk factors for Long COVID in non-hospitalized adults. *Nat Med* **28**, 1706–1714 (2022). <https://DOI.org/10.1038/s41591-022-01909-w>
2. Asadi-Pooya AA, Akbari A, Emami A, Lotfi M, Rostamihosseinkhani M, Nemati H, Barzegar Z, Kabiri M, Zeraatpisheh Z, Farjoud-Kouhanjani M, Jafari A, Sasannia F, Ashrafi S, Nazeri M, Nasiri S, Shahisavandi M. Risk Factors Associated with Long COVID Syndrome: A Retrospective Study. *Iran J Med Sci.* 2021 Nov;46(6):428-436. DOI: 10.30476/ijms.2021.92080.2326. PMID: 34840383; PMCID: PMC8611223.
3. Munipalli B, Ma Y, Li Z, et al. Risk factors for post-acute sequelae of COVID-19: Survey results from a tertiary care hospital. *Journal of Investigative Medicine.* 2023;71(8):896-906. DOI:10.1177/10815589231190560
4. Jeffrey, K., Woolford, L., Maini, R., Basetti, S., Batchelor, A., Weatherill, D., et al. (2024). Prevalence and risk factors for Long COVID among adults in Scotland using electronic health records: A national, retrospective, observational cohort study. *EClinicalMedicine.*  
<https://DOI.org/10.1016/j.eclinm.2024.102590>
5. Müller, S. A., Isaaka, L., Mumm, R., Scheidt-Nave, C., Heldt, K., Schuster, A., et al. (2023). Prevalence and risk factors for Long COVID and post-COVID-19 condition in Africa: A systematic review. *The Lancet Global Health.*  
[https://DOI.org/10.1016/S2214-109X\(23\)00384-4](https://DOI.org/10.1016/S2214-109X(23)00384-4)
6. Batiha, G.ES., Al-kuraishy, H.M., Al-Gareeb, A.I. *et al.* Pathophysiology of Post-COVID syndromes: a new perspective. *Virology* **19**, 158 (2022).  
<https://DOI.org/10.1186/s12985-022-01891-2>

7. Davis, H.E., McCorkell, L., Vogel, J.M. *et al.* Long COVID: major findings, mechanisms, and recommendations. *Nat Rev Microbiol* **21**, 133–146 (2023).

<https://DOI.org/10.1038/s41579-022-00846-2>

# Causes of Long Covid



**T**he risks listed above do not cause Long COVID. While the exact mechanisms underlying Long COVID are not entirely understood, several theories have been proposed. This section explores these theories, supported by current research findings, to provide an all-inclusive understanding of the potential biological underpinnings of Long COVID. I will concentrate on the four marked with a \* because I believe these to be the primary four causes, with everything else as secondary or contributing.

## Multiple Theories of Causes

- \* Dysautonomia/vagus nerve dysfunction
- \* Mitochondrial dysfunction
- \* Excess histamine/mast cell degranulation
- \* Gut dysbiosis
- Autoimmunity/immune dysregulation
- Thrombosis/Blood clotting
  - While I am aware of the microclots theory, because the treatment involves using clopidogrel (antiplatelet), aspirin, and apixaban (anticoagulant), which significantly increases your risk for bleeding, I have not incorporated this theory into my practice. Another reason is that the testing for microclots is not conclusive.
- Chronic inflammation

- Viral persistence – there is evidence that COVID-19 can persist in some people for up to 14 months.
  - Viral remnants – viral protein persistence
- Reactivation of latent viruses or infections (Herpes simplex, CMV, EBV, Parvovirus B19, Lyme, HHV-6A/B, varicella zoster - chicken pox)

Of course, stress and anxiety would not cause Long COVID, but it can make symptoms worse or cause flares of your symptoms.

My diagnostic and treatment protocols are not just practical and make a difference. They've brought significant improvements in health and function to many who suffer from Long COVID and COVID vaccine injuries, also known as Long vax. I hope this book will help you as much as I relished writing it.

***Why focus on just these four causes?*** When determining a cause, I assess the reliability and validity of a test or diagnosis and then consider the risks associated with the treatment. If a test or diagnosis lacks validity or reliability or the treatment poses too significant a risk, I won't use it. "First, do no harm." This principle is at the core of my practice. I take it seriously and wholeheartedly believe in it.

Each cause can elaborate on many symptoms and consequences of Long COVID, addressing downstream issues such as autoimmune disorders, immune system dysfunction, chronic inflammation, leaky gut syndrome, malabsorption, and vagus nerve dysfunction.

***Why not viral persistence?*** Viral remnants can remain persistent after recovery from acute COVID infection. These remnants, including spike proteins, are fundamental but reside inside cells. Rather than attempting the impossible task of eliminating these remnants, I focus on improving cellular health through processes like autophagy and mitophagy in damaged cells and mitochondria.

***Why not microclots?*** While clots can occur during COVID and Long COVID, the clinical significance of microclots is not transparent yet. The clots I am

concerned about—*e.g.*, deep vein thrombosis, pulmonary embolus, heart attacks, and strokes—have serious consequences. Moreover, microclots also occur in other chronic illnesses like diabetes mellitus Type 2, Alzheimer's, Parkinson's, and rheumatoid arthritis, yet patients are not routinely placed on anticoagulants or antiplatelet medications unless they're at significant risk for major clots. Triple therapy poses a severe risk of bleeding. Medications like apixaban and clopidogrel can inhibit clotting and platelets, but I believe the risk of uncontrolled bleeding outweighs the uncertain benefits of preventing microclots. Above all else, first, do no harm—this is an integral part of the *Hippocratic Oath*.

***Why not autoimmune or apheresis?*** I do consider autoimmune conditions, including autoantibodies. Doing HELP apheresis doesn't solve the cause of these antibodies, and the treatments would need to be done for the rest of your life. Apheresis can be risky because blood is removed, anticoagulated, and then reinfused. Many possible complications can occur because of this, including infections, bleeding, and clots.

***Why not reactivated Epstein Barr Virus, Lyme disease (Borrelia), Babesia, or Bartonella?*** While these can contribute to the symptoms of Long COVID, I do not believe these are a cause of Long COVID. These conditions have been found in the past in immunocompromised people, yet the presentation is significantly different from Long COVID. The symptoms of reactivated EBV can mimic some symptoms of Long Covid, but it is treated differently from Long Covid. I will address this in a later chapter. Lyme disease can remain untreated, because you didn't know you had it, or be a chronic infection. Again, this is not Long Covid, and would need to be treated as Lyme disease.

**References:**

- Su Y, Yuan D, Chen DG, Davis MM, Goldman JD, Heath JR. Multiple early factors anticipate post-acute COVID-19 sequelae. *Cell*. 2022;184(2):265-283.e18. DOI:10.1016/j.cell.2022.01.014.
- Davis, H.E., McCorkell, L., Vogel, J.M. *et al.* Long COVID: Major findings, mechanisms, and recommendations. *Nat Rev Microbiol* **21**, 133–146 (2023). <https://DOI.org/10.1038/s41579-022-00846-2>

# Questionnaire to Fill Out Before You Go to Your Doctor



1. Have you been infected with COVID-19 virus: list dates;  

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2. Have you been vaccinated against COVID-19? List dates and manufacturer if known (M=Moderna, P = Pfizer, J = Johnson & Johnson)  

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3. Do you have PoTS? MCAS? Chronic fatigue (ME/CFS)?
4. Risk factors: Have you had Lyme disease? EBV (mono)? Crohn/s disease, ulcerative colitis, celiac disease.
5. What symptoms do you currently have? (Circle all that apply)
  - a. **Systemic (entire body):** fatigue, post-exertional malaise, weakness, temperature dysregulation
  - b. **Neurological:** brain fog, concentration issues, loss of taste/smell, abnormal taste/smell, memory problems, insomnia, pins and needles, vibrations, neuropathies, dizziness, numbness, headaches, tinnitus, seizures, tremors
  - c. **Psychiatric:** anxiety, irritability, depression, PTSD, tearfulness
  - d. **Cardiovascular** (heart/blood): tachycardia, palpitations, chest pain, inflamed blood vessels

- e. **Pulmonary** (lungs): shortness of breath, dry cough, breathing difficulty
- f. **Ear, nose, eyes, and throat:** sore throat, blurry vision/change in vision, lump in throat/hoarseness, sensitivity to light or sound
- g. **Gastrointestinal:** abdominal cramps, bloating, diarrhea, nausea/vomiting, GERD
- h. **Dermatologic** (skin): rashes, petechiae, itchy skin
- i. **Musculoskeletal:** chest tightness, muscle aches, joint pains, muscle spasms
- j. **Reproductive:** period changes, heavy periods, sexual dysfunction, bladder control issues, testicular pain.
- k. **Immunologic:** increased allergies, new allergies, shingles, EBV reactivation

**6. What blood work have you had? (circle)**

- a. CBC with differential, basic metabolic panel, liver function tests, D-dimer, CRP, TSH, Free T3, Homocysteine level, HbA1C, Troponin, pro-BNP, vitamin D, vitamin B12, ferritin, 24hr urine N-methylhistamine, ANA, lupus anticoagulant.

**7. What over-the-counter supplements have you tried? (do not list anything not on the list)**

- a. Resveratrol, quercetin, co Q-10, omega 3 fatty acids, magnesium, vitamin D, vitamin B12/B complex, NAC, melatonin, probiotics, nattokinase/serropeptase/lumbrokinase, bromelain, L-arginine, L-citrulline, vitamin C, nigella sativa (black seed oil), PEA/luteolin, curcumin, lactoferrin, selenium, zinc, iron.

**8. What prescription medications have you tried?**

- a. Guanfacine, Mestinon (pyridostigmine), Low-Dose Naltrexone (LDN), ivermectin, hydroxychloroquine, colchicine, Cetirizine (Zyrtec), famotidine/Pepcid, nadolol, midodrine, antidepressants,

benzodiazepines, Maraviroc, Paxlovid, triple anticoagulant therapy (Clopidogrel 75mg + Aspirin 75mg) once a day, and a direct oral anticoagulant (Apixaban) 5mg twice a day. pantoprazole 40 mg/day for gastric protection.

Other: \_\_\_\_\_

9. Do you use a vagus nerve stimulator?
10. Have you tried the nicotine patch?
11. Have you had an SGB (stellate ganglion block)?
  - a. Was it 1 level or 2 (one-shot or 2 on the same side)?
  - b. Was it done with an ultrasound?
  - c. Did you have *Horner's* syndrome (red eye, small pupil, droopy eye, stuffy nostril)?
12. What other treatments have you tried?