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THE NATUROPATH'S GUIDE

LONG COVID

A focus on the herbal approach for managing long COVID

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LIQUORICE
(Glycyrrhiza glabra)

LONG COVID

Long COVID, one of the colloquial terms for post coronavirus disease 2019 (COVID-19) condition, is an umbrella term used to describe chronic outcomes of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the virus that causes COVID-19

Most people who develop COVID-19 fully recover however current evidence suggests approximately 10% to 20% (recent studies indicate it could be even higher at more than a third) of people experience a variety of lasting symptoms after they recover from their initial illness. This can include fatigue, shortness of breath and neurological complaints such as cognitive dysfunction. Some people also experience psychological effects as part of long COVID. These symptoms might persist from their initial illness or develop after the typical convalescence period. They can wax and wane or relapse over time. People who experience long COVID sometimes refer to themselves as "long-haulers".

Condition Overview

During the early stages of the pandemic the general public appeared to be concerned about the fatality of COVID-19 and, later on, the psychological and social consequences of the pandemic were highlighted. More recently the lingering symptoms following the acute phase of the disease have been recognised and this puzzling, long COVID phenomenon has been dubbed the "pandemic after the pandemic".

The term long COVID was first used in May 2020 by Elisa Perego, from the Institute of Archaeology at University College in London, as a Twitter hashtag to describe her own experience of the condition. However it is not the only term being used to describe persistent symptoms. Other terms include post-acute sequelae of SARS-CoV-2 infection (PASC), post-COVID-19, post-acute COVID-19 syndrome, chronic COVID syndrome and chronic COVID-19.

The World Health Organization (WHO) has developed a clinical case definition of long COVID:

"Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually three months from the onset of COVID-19 with symptoms and that last for at least two months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time."

This first version of a definition was developed by patients, researchers and others, representing all WHO regions, with the understanding that it may change as new evidence emerges and the understanding of the consequences of COVID-19 continues to evolve. Critics say the WHO's definition of long COVID is vague, which leads to concerns that a variety of conditions, including psychosomatic

complaints, become intermixed with more severe, post-infectious organ dysfunction.

Each case of COVID-19 is unique and each person will have a different experience in their recovery. Some people may recover in days, some in weeks and for others it could be months. Some people are infected by SARS-CoV-2 and never get sick while others suffer damage to their immune system and ongoing inflammation. As such there are different categories of long COVID. Some people have direct cell damage because of the virus and this can cause lingering symptoms where they do not recover completely. When a person's symptoms are related to chronic hospitalisation, and recovering from severe COVID-19, they may have lung or other organ damage as a result of pneumonia or acute respiratory distress syndrome, muscle weakness, cognitive brain dysfunction or they may have lingering symptoms consistent with post-intensive care unit syndrome, which is a post-traumatic stress disorder-like syndrome. Then there are those cases in which symptoms appear after recovery reflecting the interplay between inflammatory markers and the immune system.

Long COVID can be difficult to identify because many of its symptoms are similar to those of other diseases and conditions. It is also difficult to predict what length of time long COVID will last for any given patient. There is much to learn about it, but current research shows that patients can experience lingering symptoms for weeks to months following COVID-19. The research also shows that patients can improve with time. The symptoms can affect a person's ability to perform daily activities such as work or household chores. This can leave patients feeling helpless and alone in managing their symptoms. Australian data confirms that people with long COVID have reported significant stigma, difficulties in accessing services and returning to full time work, trouble maintaining important relationships and life roles and barriers to engaging in activities of daily living.

To understand long COVID first it is important to understand how SARS CoV-2 infects. Put simply the cellular entry point for SARS CoV-2 is when it binds to the angiotensin converting enzyme-2 (ACE2) receptor. Attachment of the virus to the ACE2 receptor is associated with increased levels of angiotensin leading to inflammation, vasoconstriction and thrombosis. In addition to the ACE2 receptor, SARS-CoV-2 requires a protease (enzymes that break down protein) to prime the famous spike protein before the virus can enter the cell. The ACE2 receptor and the required protease are both expressed in lung, heart, gut smooth muscle, liver, kidney, neurons and immune cells which provide an explanation for the symptomatology of COVID-19.

It is postulated that severe long COVID symptoms can be traced back to the loss of ACE2 activity, even in those who did not get sick. Loss of ACE2 can cause problems with energy metabolism and mitochondria (the energy producing powerhouses inside cells), and result in cardiac problems, pneumonia, blood clots, kidney failure, strokes, seizures, brain fog, excessive inflammation and autoimmune disease. There is an abundance of ACE2 receptors in the gastrointestinal tract as well, and COVID-19 commonly produces gut dysbiosis. This allows pro-inflammatory bacteria to thrive in the gut microbiome and contributes to other inflammatory symptoms. Long COVID is not only seen after COVID-19 infection but it is being observed in some people that have received COVID-19 vaccines (possibly due to autoantibodies to the ACE2 receptor, which the spike protein targets).

Why long COVID symptoms persist is unclear at this time, and the research is complicated, although there are a number of hypotheses. An ongoing study, published in the Annals of Internal Medicine on 24 May 2022, compared 189 patients diagnosed with COVID-19 to 120 similar patients who did not get sick. The researchers found that an extensive medical evaluation failed to reveal a cause for persistent symptoms in most cases. The infectious disease specialist who led the study said they were not able to find evidence of the virus persisting or hiding out in the body. They also did not find evidence that the immune system was overactive or malfunctioning in a way that would produce injury to major organs in the body. The researchers did, however, find that women and those suffering from anxiety were more likely to end up with long COVID.

Many experts say long COVID likely results from a variety of disease-causing mechanisms, so its expression is highly varied, and depends on factors such as an individual's predisposing

characteristics and different underlying biological factors driving their symptoms, none of which are mutually exclusive. Common theories include viral persistence, inactivated viral fragments or reactivation of a latent virus. While research is still ongoing to make any conclusive statements it is believed to possibly be caused by an immune state triggered by pro-inflammatory cytokines. Several studies have reported that adaptive immunity and pro-inflammatory cytokines become increased in patients with COVID-19 as the virus causes systemic inflammation. This mechanism plays a crucial role in immune regulation. Some of the hypotheses and potential contributors to long COVID symptoms include:

Viral Persistence

The COVID-19 virus could still be lingering in the body in a reservoir site and patients are still being exposed to COVID-19 antigens. In more technical terms this could be monocyte and microglia activation. Persistence of viral debris (possibly spike protein) in monocytes and microglia results in an ongoing inflammatory response in an attempt by the immune system to clear the offending protein(s) and viral ribonucleic acid (RNA) fragments.

Autoimmune

The virus triggers some sort of autoimmune process that persists which could be due to molecular mimicry between pathogen and host proteins.

Tissue Injury

There is some viral-induced tissue injury or damage to one or multiple organs and this is a persistent post-inflammatory response as a result.

Hyperinflammation

Mast cells are a type of white blood cell found in connective tissue throughout the body. They produce allergy-related symptoms and can be activated by SARS-CoV-2 infection. It has been suggested that hyperinflammation caused by COVID-19 may be mediated by mast cell activation which may cause long COVID symptoms such as neurodegeneration and cognitive decline. The similarity between mast cell activation syndrome (causing allergy symptoms) and long COVID has been observed. Mast cells are present in the brain. Following stimulation they release proinflammatory mediators, such as histamine and cytokines, which may result in neurovascular inflammation. The brain fog, cognitive impairment and general fatigue reported in long COVID may be due to mast cell related neurovascular inflammation.

Reactivation of Pathogens

Dormant viruses in the body can be reactivated by COVID-19. These dormant viruses include the Epstein-Barr virus (EBV) (that causes glandular fever), the chickenpox virus (that can cause shingles) as well as human herpesvirus 6, which causes herpes simplex viruses, herpes zoster, as well as the common childhood illness sixth disease. These viruses can be harmless and symptomless, kept at bay by a healthy immune system, until reactivated by things such as an infection or stress.

Unresolved Pneumonia

Ongoing respiratory symptoms (shortness of breath, cough, reduced effort tolerance) may be related to a type of pneumonia that is unresolved.

In summary, long COVID seems to be a puzzle of multiple syndromes after the acute infection phase. In the words of neuroscientist Avindra Nath: “Modern medicine has faced its biggest challenge from the smallest of organisms.”

A May 2022 study recognises that SARS-CoV-2 is not unique in its ability to cause aftereffects following the acute illness. Other acute infections have long been associated with an unexplained chronic disability in a minority of patients. Although known for a long time, little attention has been paid to the chronic effects described in a proportion of exposed individuals following infections such as Epstein-Barr virus (EBV), dengue fever, Ross River virus, influenza A, Ebola and perhaps Lyme disease. The relatively similar symptom profiles of individual post-acute infection syndromes (PAISs), irrespective of the infectious agent, as well as the overlap of clinical features with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS: a condition that can follow viral illnesses and leads to debilitating exhaustion), suggest the potential involvement of a common cause. Up to 75% of ME/CFS cases report an infection-like episode preceding the onset of their illness. It has repeatedly been found that a proportion of people

with PAISs triggered by various pathogens fulfill the diagnostic criteria for ME/CFS. Long COVID shares several key characteristics with ME/CFS and chronic Lyme disease. These include problems with mitochondrial function, fatigue, brain fog and muscle pain. Despite the significant worldwide impact of such chronic illnesses they often go undiagnosed owing to the nonspecific nature of symptoms and a lack of objective diagnostic findings. All manner of infectious agents, including bacteria, viruses and parasites, has been implicated in the development of PAIS. Unfortunately the association between acute infectious diseases and unexplained chronic disability remains understudied which leads to poor recognition of these conditions in clinical practice. As a result patients might experience delayed or a complete lack of clinical care. The researchers said "the SARS-CoV-2 pandemic uncovered a significant gap in knowledge about post-acute sequelae of infectious diseases and identified the need for better diagnostic care and clinical infrastructure for patients experiencing these long-term effects. The unprecedented amount of attention and resources that have recently been allocated to the study of COVID-19-related pathology brings a promise of much needed progress in the wider field of unexplained infection-associated chronic disability.

Common Symptoms

The most common side effects of long COVID appear to be fatigue and shortness of breath, often lasting for months after the initial infection. Other persistent symptoms may include:

Pulmonary

- Difficulty breathing
- Chest pain
- Persistent cough
- Sore throat, trouble speaking

Cardiovascular

- Myocarditis/ pericarditis
- Heart attack
- Irregular heartbeat

Endocrine

- Deterioration of diabetic control
- Osteoporosis due to prolonged immobilisation

Mental Health

- Cognitive decline such as confusion, forgetfulness, lack of mental focus and clarity
- Depression
- Anxiety
- Insomnia, sleep problems
- Post-traumatic stress disorder following severe illness

Neurological

- Brain fog
- Cognitive impairment
- Long term fatigue
- Headaches
- Loss of smell or taste
- Pins and needles
- Dizziness
- Epilepsy
- Stroke

Haematological

- Anaemia
- Blood clots in the veins

Musculoskeletal

- Muscle aches, pains and weakness
- Inability to exercise
- Joint stiffness

Dermatological

- Skin rashes
- Hair shedding

General

- Reduced nutritional status and weight loss
- Low-grade fevers
- Renal impairment
- Gastrointestinal upset
- Liver dysfunction
- Pressure sores
- Reduced quality of life

Risk Factors

Anyone who becomes ill with COVID-19 can develop long COVID. Long COVID is being studied by many experts around the world and the knowledge and understanding of it is growing. There does not appear to be a relationship between the initial severity of COVID-19 infection and the likelihood of developing long COVID.

Sex

Females appear to be at greater risk than men. Vulnerability to, and mortality from, acute COVID-19 infection is higher in men, whereas long COVID disproportionately affects women pointing towards sex hormone differences as targets for further investigation. Many symptoms of long COVID have a significant overlap with perimenopause and menopause. Such overlap may create diagnostic uncertainty and could lead to women with symptoms of perimenopause and menopause being misdiagnosed with long COVID.

Age

In research long COVID is more likely correlated with increasing age.

EBV

There is research to suggest that many long COVID symptoms may not be a direct result of the SARS-CoV-2 virus but may be the result of COVID-19 inflammation-induced EBV reactivation. EBV is the virus that causes glandular fever.

Vagus Nerve Dysfunction

According to research several long COVID symptoms (including long-term issues with voice, difficulty swallowing, dizziness, a high heart rate, low blood pressure and diarrhoea) could be linked to the damaging effects of COVID-19 (possibly inflammation) on the vital central nerve, the vagus nerve. The vagus nerve, which runs from the brain into the body, connects to the heart, lungs, intestines and several muscles involved with swallowing. It plays a role in several body functions that control heart rate, speech, the gag reflex, sweating and digestion.

Pre-existing Conditions (with meta-analyses evidence)

Cancer, it can take some time (from nine months up to 12 years) for the immune system to recover from chemotherapy, cerebrovascular disease, chronic lung disease, chronic liver disease, heart conditions, mental health disorders (depression and schizophrenia spectrum disorders), obesity and diabetes type 1 and 2 (both associated with proinflammatory cytokines), pregnancy, smoking (both current and former because of damage to lungs) and tuberculosis.

Pre-existing Conditions (with observational studies)

Children with certain underlying conditions, Down syndrome, human immunodeficiency virus (HIV), neurologic conditions including dementia, being overweight (BMI > or equal to 25kg/m2 but <30kg/m2), sickle cell disease, solid organ or blood stem cell transplantation, substance use disorders, use of corticosteroids or other immunosuppressive medications.

Pre-existing Conditions (mixed evidence)

Cystic fibrosis, thalassemia, asthma, hypertension (possibly in pregnant and non-pregnant women), immune deficiencies.

Microbiome

Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19. In some studies patients with COVID-19 were depleted in gut bacteria with known immunomodulatory potential including *Faecalibacterium prausnitzii, Eubacterium rectale* and several bifidobacterial species (which produce short chain fatty acids which can reduce disease and inflammatory cytokines). The dysbiotic gut microbiota composition in patients with COVID-19 continues after clearance of the virus which could contribute to persistent symptoms.

Vaccination

A huge study has shown that long COVID risk falls only slightly after vaccination highlighting the importance of the naturopathic principle of prevention, which is the focus on health as well as disease. The prevention of disease, and the attainment of optimal health in patients, are primary objectives of naturopathic medicine. In practice, these objectives are accomplished through education and the promotion of healthy ways of living. According to the study of more than 13 million people, published on 25 May 2022, vaccination against SARS-CoV-2 lowers the risk of long COVID after infection by only about 15%. “Altogether, the findings suggest that vaccination before infection confers only partial protection in the post-acute

phase of the disease; hence, reliance on it as a sole mitigation strategy may not optimally reduce long-term health consequences of SARS-CoV-2 infection," the American researchers said.

How To Get The Correct Diagnosis

The definition and mechanism of long COVID is still unclear however it is considered, by default, to be a diagnosis of exclusion. At present (May 2022) the minimum time before a person is diagnosed with long COVID-19 is usually three months after they first developed symptoms of COVID-19. The three-month time period rules out the normal recovery process after illness. Alternative explanations for symptoms need to be ruled out before associating the symptoms with long COVID.

These clinical case definitions (see table below) are used to identify and diagnose the long-term effects of COVID-19.

The term long COVID is commonly used to describe signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from four to 12 weeks) and post-COVID-19 syndrome (12 weeks or more).

Conventional Treatment & Prevention

Long COVID is a relatively unknown syndrome and one that benefits from multidisciplinary management. At present there is no specific medication therapy for people with it. The absence of a clear biomarker makes chronic conditions like this (post infection inflammatory syndromes such as long COVID, ME/CFS and chronic Lyme disease) challenging for many conventionally trained doctors. There is data suggesting that holistic care, including rehabilitation, can be helpful. Post-COVID-19 care centres are opening at many academic medical centres. If a COVID-19 care centre is available patients are referred. If a COVID-19 care centre is not available specialists are consulted. Given the impact on mental health, evaluating the mental health of people with long COVID is a priority.

Clinics for long COVID patients have already opened in parts of Australia including at public hospitals in Sydney, Melbourne, Canberra and Adelaide. On 30 March 2022, St Vincent's Hospital in Sydney was the first hospital in New South Wales to open a dedicated post-acute multidisciplinary long COVID

Clinical Case Definitions

Type	Definition
Acute COVID-19	Signs and symptoms of COVID-19 for up to four weeks.
Ongoing symptomatic COVID-19	Signs and symptoms of COVID-19 from four weeks up to 12 weeks.
Post-COVID-19 syndrome	Signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis. It usually presents with clusters of symptoms, often over-lapping, which can fluctuate and change over time and can affect any system in the body. Post-COVID-19 syndrome may be considered before 12 weeks while the possibility of an alternative underlying disease is also being assessed.

clinic to manage patients still suffering the effects of COVID-19 months after testing negative to the virus. To support general practitioners, and the community, with persistent post-COVID symptoms the outpatient clinic is designed to carefully manage and minimise long term symptoms and, ultimately, facilitate patients' return to work or school. The team includes respiratory and rehabilitation specialists, nursing, physiotherapy and psychology to support a holistic recovery from this new and complex disease. The main allopathic treatments for long COVID, currently being utilised at St. Vincent's Hospital in Sydney, are rehabilitation, treating the post-viral inflammatory fatigue, cognitive therapy (if struggling with mental health) and assessing lung and heart function.

Patients might be fearful of stigmatisation of their COVID-19 infection and ongoing symptoms. Doctors have been instructed to ensure their patients understand that having some post-COVID-19 symptoms does not mean they are still infectious.

"Modern medicine has faced its biggest challenge from the smallest of organisms."

Neuroscientist
Avindra Nath

St John's Wort
(Hypericum perforatum)

INTERVENTION	Adaptogen etc.	Anti-inflammatory	Antiviral (antimicrobial)	Antioxidant	Immune modulator	Cardioprotective, circulatory stimulant
Astragalus	✓		✓	✓	✓	✓
Codonopsis	✓	✓			✓	
Echinacea		✓	✓	✓	✓	✓
Garlic		✓	✓	✓	✓	✓
Ginkgo	✓	✓	✓	✓		✓
Lemon Balm	✓	✓	✓	✓		
Liquorice	✓	✓	✓	✓	✓	
Nigella	✓	✓	✓	✓	✓	✓
Perilla	✓	✓		✓		
Reishi	✓	✓	✓	✓	✓	
St. John's Wort	✓	✓	✓			
Withania	✓	✓		✓	✓	✓

Natural Therapies For Treatment & Prevention

The adage "an ounce of prevention is worth a pound of cure" applies to long COVID. The best way to protect against it is to avoid getting infected with the SARS-CoV-2 virus. However, with the virus being highly contagious, many people will catch it and be at risk of developing long COVID. It is therefore becoming a growing niche area in clinical practice. There is no magic bullet for the condition so treatment comes down to managing individual symptoms with different therapeutic approaches and providing supportive care. Strengthening immunity, along with maintaining healthy living, is the best way to survive COVID-19 and long COVID.

It is encouraging to see academic medical journals suggest that long COVID patients require an integrative health approach, one that combines traditional medical management, non-pharmacological approaches and behaviour and lifestyle changes.

Long COVID is a complex, multifactorial condition and is an opportunity to address other comorbidities. While it can present a larger, and more varied, constellation of symptoms than ME/CFS or chronic Lyme disease, it may respond well to the same tools used to address these conditions. Treatment aims to manage not only the fatigue itself but any number of causative factors from viruses and other microorganisms to inflammatory and immune abnormalities, gut dysfunction and dysbiosis and circulatory, cognitive, hormonal and biochemical factors.

Beyond the science, taking a naturopathic approach to post-viral chronic fatigue the primary prescription would be convalescence, maximising self-care, sleep, relaxation, sunshine, gentle exercise, fresh air and nutrition. It will take time. According to the renowned herbalist Simon Mills "the neglect of convalescence may yet prove to be one of the most serious mistakes of modern medicine." The seminal herbal textbook, Principles and Practice of Phytotherapy, says: "A good convalescence is a marvellous thing. It rounds off an illness and gives it meaning; it makes the sufferer stronger for having had the illness. In a way no vaccination could do, it arms and strengthens the immune defences and provides real protection against recurrence, possibly forever...".

Through careful case taking and monitoring, practitioners will collaborate with their patient to develop an individualised management plan, and unique protocol, to support their recovery. A focused plan of action can be achieved by identifying specific symptoms in the context of the patient's unique environment, lifestyle, triggers and history focusing on the foundations of health including diet, lifestyle and exercise.

Naturopath's and herbalists will also take into consideration dysbiosis, which is becoming more likely as a suspect for why people are experiencing long COVID. According to a leading researcher in the field of integrative medicine, Professor of Immunology Dr Heather Zwickey, long COVID indicates the need to restore dysbiosis to a state of health. She says when there is dysbiosis there is a reduction of commensal bacteria (normal microflora) or an overgrowth of some species of commensal bacteria which become pathogenic. When this happens there is less mucous production which can cause poor intestinal barrier integrity and consequently inflammation which can cause anxiety, depression and fatigue. The physical damage to the gut can cause malabsorption of nutrients which can lead to nutrient deficiency causing stress. "When you feed your microbiome your microbes, in your microbiome, make metabolites and those metabolites, like short chain fatty acids [neurotransmitters and amino acids], impact the immune response. The more diverse the microbes are in your microbiome the more metabolites you're going to make and the healthier you are. This is called alpha diversity. So what we like to say is that people with high alpha diversity are going to be healthier," she says.

In summary, a focused strategy would involve encouraging the consumption of a clean and healthy diet together with the intake of high quality herbal and nutritional substances for immunomodulation and inflammation reduction. The key treatment goals include addressing:

- Dysbiosis
- Inflammation
- Mitochondrial dysfunction and boost immune function

- Endothelial and microcirculatory dysfunction
- Metabolic imbalances and insulin resistance
- Potential viral reservoir
- Malnutrition
- Energy levels and mood

Diet

It is of paramount importance to encourage the adoption of healthy eating habits. Diet can be a source of inflammation so whatever can be done to lower inflammation will allow the immune system to work better. Dietary changes can be the first step to easing inflammation and oxidative stress, supporting ACE2 activity and improving mitochondrial function. A diet that is anti-inflammatory and rich in flavonoids will help create a healthier gut microbiome. Focus on whole foods rich in protein, fibre, healthy fats and the micronutrients the immune system needs to thrive. Non-processed, whole foods should be foundational in the recovery diet. Upgrading the intake of quality (organic/seasonal) fruits and vegetables is key. What is added is as important as what is avoided.

The Mediterranean Diet

Having high antioxidant, anti-inflammatory and potential antimicrobial and immunomodulatory properties the Mediterranean diet may address both short- and long-term conditions associated with COVID-19. Reputed for its demonstrated preventive effects on cardiovascular diseases and type-2 diabetes in several trials, it is characterised by the inclusion of mainly plant-derived nutritional components including fruits, vegetables, legumes, nuts and olive oil.

Adequate Protein

To help with immune recovery, neuroinflammation, reduced neurotransmitters, and to address any malnutrition there is a need to ensure adequate intake of nutrients and amino acids including tryptophan, tyrosine and arginine from meats. Include oily fish, nuts, chia, flax seeds and seeds rich in anti-inflammatory essential fatty acids to assist with cognitive function and to help to resolve infection.

Increased Dietary Fibre Correlates with Increased Microbial Diversity

This includes prebiotics (food that feeds the microbes) such as leeks, onions, garlic, asparagus, Jerusalem artichoke, banana, mushrooms, cayenne, cinnamon, ginger, rosemary, turmeric, black pepper, oregano; probiotics (live bacteria) and fermented foods.

Plant Foods

One study has revealed that the diversity of plants that a person consumes is associated with microbial diversity. Consuming more than 30 types (not servings) of plants (spices, nuts and grains are plants as well as fruits and vegetables) per week, and consuming more vegetables and fruits, was associated with a higher abundance of conjugated linoleic acid which is generally related to reduced inflammation and cardiovascular disease, and a reduction in certain antibiotic resistant genes. This means the more diverse a person's plant intake is the more diverse their alpha diversity is. The fact that microbial communities tend to group by macronutrient and micronutrient intake levels in a person's diet, rather than by diet type, highlights the contribution of dietary nutrients in regulating gut microbial metabolism.

Probiotics

Used to help with dysbiosis. Emerging evidence implies that general susceptibility to infectious agents may be diminished by probiotic interventions. More specifically the use of probiotics may manipulate intestinal microbiota and, in turn, modulate the immune system and its inflammatory responses.

Supporting a Good Nutrient Baseline

Insufficient levels of zinc and selenium are associated with worse outcomes from viral infections. Good sources of zinc include oysters, hemp seeds and pumpkin seeds, beans, nuts and animal protein. Sources of selenium include mushrooms, Brazil nuts and seafood. Quercetin is a flavonoid found in dill, broccoli, onions, capers, apples and berries. It is a mast-cell stabiliser useful for people who have allergies, asthma and mast-cell issues. It appears to bind to the spike protein

of SARS-CoV-2, inhibit inflammatory pathways and block replication of infected cells. Include eight to 12 servings of phytonutrients a day from vegetables, fruits, spices, herbs and tea, cruciferous vegetables (such as kale, broccoli and cabbage), avocado, spinach and the onion family, which can help bolster levels of glutathione. Antioxidants from food sources are essential for cellular health which is of utmost importance when the body has increased demands such as in illness recovery.

Intermittent Fasting

Intermittent fasting, or time-restricted eating, can help rejuvenate the immune system. Restricting feeding to shortened windows helps stimulate the removal of damaged mitochondria. Fasting also supports the turnover of damaged cells throughout the body making room for new, healthy mitochondria and cells to take their place. Time-restricted eating can take a variety of forms. One of the most popular is simply eating all the day's meals within an eight-hour window, then going 16 hours without food or calories.

Hydrate

Stay hydrated and drink before feeling thirsty.

Avoid

Intake of refined carbohydrates, stimulants such as caffeine which may delay recovery, alcohol and foods containing preservatives, additives, sugar and artificial sweeteners which may impair immunity.

Food Allergies or Intolerances

Identify and eliminate any food allergies or intolerances so there is less stress on the immune system.

Lifestyle

Mindfulness Plan

This helps reduce stress, and other mood deviations, and could include counselling, yoga, journaling, meditation, guided imagery and breathing exercises. The breathing exercises not only help with anxiety and stress but can improve the breathlessness post-COVID patients often feel, particularly those who are left with pulmonary fibrosis.

Support Sleep Hygiene

Ensure the patient is getting plenty of rest. Circadian rhythm is key to healthy, rejuvenating rest. Something as simple as normal daylight and moonlight exposure can restore this rhythm.

Caution with Return to Exercise

A monitored return to exercise can be supported by an exercise physiology, physiotherapy or rehabilitation referral. Avoid strenuous exercise. Gentle restorative activity such as beach or bush walking, tai chi or yoga are suitable. Exercise up to the appropriate tolerance, slowly building as energy increases, and reduce if there is any increase in symptoms. Combine resting and napping with appropriate activity. A relaxing bath in Epsom salts with lavender essential oil could help with muscle aches and sleep.

Acupuncture

Appears to be helpful for people with long COVID.

Remove the Toxic Load

Being diligent about decreasing exposure to toxins (including alcohol) and pollutants is highly beneficial. Supporting a healthy gut is central to excreting toxins, preventing inflammation and curbing symptoms. Microbes can be killed by chemicals, preservatives and medications (both antibiotic and nonantibiotic).

Steam Inhalations

For respiratory issues.

Social Connection and Purpose

Being both socially isolated and feeling lonely is associated with chronic inflammation. Keep in touch with loved ones and pursue enjoyable activities such as learning something new or adopt a pet.

Potential Treatment Plans

Long COVID	Astragalus	Reishi	Perilla	Nigella	Codonopsis
Long COVID with fatigue	Astragalus	Liquorice	Withania	Reishi	Codonopsis
Long COVID with brain fog	Echinacea	Ginkgo	Garlic	Withania	Lemon Balm
Long COVID with depression	Garlic	St. John's Wort	Lemon Balm	Codonopsis	Perilla

Ginkgo
(Ginkgo biloba)

Desired Herbal Actions and Potential Herbs Include:

Given long COVID has a broad spectrum of symptoms, and can affect any body system, it is not within the scope of this paper to cover every action which may apply. Rather, an overview of the most relevant actions has been attempted with the understanding that practitioners will consider other actions where appropriate.

Adaptogen, Nervines, Neuroprotective, Antidepressant, Anxiolytic, Adrenal Support, Nutritive and Tonic Herbs

Increase energy levels, stabilise mood, reduce depression and stress (long and short term) and assist general strength. Support the hypothalamic-pituitary-adrenal (HPA) axis dysregulation which can be a driver for stress. Herbs such as angelica, astragalus, bacopa, codonopsis, ginkgo, gotu kola, holy basil, Korean ginseng, lemon balm, liquorice, maritime pine, muira puama, nigella, perilla, rehmannia, reishi, rhodiola, saffron, St. John's wort, schizandra, Siberian ginseng, turmeric, vervain, withania.

Nutritive and tonic herbs replenish minerals and vitamins spent during an illness. Herbs such as alfalfa, fenugreek, nettle leaf, oats green, rose hips.

Bitter tonics, such as gentian and dandelion root, speed recovery by stimulating the appetite as well as digestion.

Anti-inflammatory

Reduce inflammation. Whether persistent interleukin (IL)-6 (a proinflammatory cytokine) dysregulation and/or activity of other inflammatory markers contributes to COVID-19-related long-term fatigue, sleeping difficulties and depression or anxiety is an important theory that requires investigation. Herbs such as albizia, arjuna, astragalus, bacopa, baical scullcap, bupleurum, cat's claw, codonopsis, echinacea, elecampane, feverfew, garlic, ginkgo, ginger, gotu kola, hemidesmus, holy basil, ivy leaf, lemon balm, liquorice, magnolia, maritime pine, nigella, perilla, pomegranate, rehmannia, reishi, rhodiola, rosemary, St. John's wort, turmeric, willow bark, withania.

Antiviral (antimicrobial)

Eradicate any infection. Herbs such as albizia, arjuna, astragalus, bupleurum, cat's claw, echinacea, elecampane, feverfew, garlic, ginkgo, glossy privet, golden seal, ginger, holy basil, ivy leaf, lemon balm, liquorice, magnolia, nigella, reishi, St. John's wort, sweet wormwood, thuja, turmeric.

Antioxidant

Especially plants with protective activity on the microvasculature. Herbs such as albizia, arjuna, astragalus, bacopa, bilberry, cat's claw, echinacea, dandelion leaf, garlic, ginkgo, glossy privet, gotu kola, green tea, holy basil, lemon balm, liquorice, magnolia, maritime pine, nigella, perilla, pomegranate, reishi, rosemary, sage, turmeric, withania.

Immune Modulator

Long COVID can take its toll on the immune system so herbs that build white and red blood cells have a part in convalescence. Herbs such as andrographis, astragalus, cat's claw, codonopsis, echinacea, elderberry, garlic, ginkgo, glossy privet, holy basil, liquorice, nigella, reishi, schizandra, withania.

Cardioprotective, Circulatory Stimulant

Support any cardiac and circulatory abnormalities and improve cognition. Herbs such as arjuna, astragalus, bilberry, butcher's broom, echinacea, ginkgo, garlic, ginger, gotu kola, hawthorn, holy basil, horsechestnut, maritime pine, motherwort, nigella, prickly ash, withania.

Herbal Support Could Include:

HERB NAME	DESCRIPTION	ACTIONS
Astragalus *(Astragalus membranaceus)* 	Astragalus has been used traditionally to build and support immunity, assist with post-disease fatigue and digestion. It is a gentle herb to use in the later stage of recovery. In Traditional Chinese Medicine theory astragalus regulates the blood (vital energy), preparing the flow of blood to fight against the attack of pathogens and strengthen the body defences. It has also been prescribed for chronic fatigue syndrome.	Immune Modulator Antioxidant Cardioprotective Adaptogen Antiviral
Codonopsis *(Codonopsis pilosula)* 	Historically codonopsis has been used as a low cost replacement for Korean ginseng *(Panax ginseng)* and is also known as 'poor man's ginseng'. With similar actions to Korean ginseng and Siberian ginseng *(Eleutherococcus senticosus)*, codonopsis is an immune tonic and adaptogen useful for fatigue. It is used as support during convalescence and can be used to return vitality to pre-illness levels. Codonopsis is useful for conditions associated with chronic fatigue, especially of the variety that interferes with digestion and assimilation, or causes symptoms of shortness of breath and heaviness in the limbs.	Immune Modulator Adaptogen Anti-inflammatory
Echinacea *(Echinacea purpurea)* 	In an April 2022 randomised, open, controlled, exploratory clinical study *E. purpurea* exhibited antiviral effects, by substantially reducing virus loads in infected people, and reduced the risk of viral respiratory tract infections, including SARS-CoV-2. There were also fewer Covid-19 related hospitalisations in the *E. purpurea* treatment group.	Immune Modulator Modulates Inflammation Antimicrobial Circulatory Stimulant Antioxidant
Garlic *(Allium sativum)* 	Garlic has traditionally been used to support the immune system, the heart and intestinal health. It appears to enhance the functioning of the immune system by stimulating certain cell types such as macrophages, lymphocytes, natural killer cells, dendritic cells and eosinophils by mechanisms including modulation of cytokine secretion, immunoglobulin production, phagocytosis and macrophage activation.	Antimicrobial Immune Modulator Anti-inflammatory Antioxidant Circulatory Stimulant

Herbal Support Could Include: (Cont.)

HERB NAME	DESCRIPTION	ACTIONS
Ginkgo *(Ginkgo biloba)* 	It is hypothesised that microvascular dysfunction is a mechanism for the neurological problems of long COVID. The available data suggests a similar underlying pathology in viruses other than SARS-CoV-2. This theory provides a rationale for therapies targeting microvascular regeneration to relieve symptoms caused by vascular injury and reduced blood flow due to long COVID. This suggests ginkgo, which improves blood flow, would be beneficial as there is clear evidence to support its efficacy for mild cognitive impairment and dementia. Numerous clinical trials demonstrate that ginkgo improves memory loss, and concentration, and decreases anxiety in patients with dementia and/or vascular dementia.	Antioxidant Anxiolytic Nootropic (Cognitive Enhancer) Neuroprotective Cardioprotective Anti-inflammatory Circulatory Stimulant (Cerebral) Antimicrobial
Lemon Balm *(Melissa officinalis)* 	Addressing some of the most common symptoms of long COVID, lemon balm has traditionally been used for “all complaints supposed to proceed from a disordered state of the nervous system”. It can also improve cognitive performance and mood. It may also help conditions related to oxidative stress, which may assist the cardiovascular involvement of long COVID. The results of a 2018 double blind placebo controlled clinical trial showed that eight weeks supplementation with 3g of lemon balm can decrease anxiety, depression, stress and sleep disorder in patients with chronic stable angina. There is preclinical evidence to show that some of lemon balm’s constituents have an antiviral affect against the main protease and spike protein of COVID-19, Avian influenza (bird flu), HIV-1 and enterovirus.	Relaxing Nervine Anxiolytic Antidepressant Sedative Nootropic Nervine Tonic Antimicrobial Antiviral Anti-inflammatory Antioxidant
Liquorice *(Glycyrrhiza glabra)* 	Suboptimal function of the HPA axis has been implicated in long COVID and ME/CFS. Liquorice has restorative effects on the adrenal glands and has been shown to help support HPA axis balance by impacting morning cortisol levels. This is important because chronically low cortisol levels can put stress on adrenal function. Liquorice also supports healthy immunity and inflammation.	Anti-inflammatory Antioxidant Adrenal Tonic Antiviral Antimicrobial Immune Modulator

Herbal Support Could Include: (Cont.)

HERB NAME	DESCRIPTION	ACTIONS
Nigella *(Nigella sativa)* 	The seeds of nigella have been used for centuries as a traditional remedy for multiple medical conditions, including inflammation and infections. Australian scientists say there is growing evidence from modelling studies that constituents in nigella can stick to the COVID- 19 virus spike protein, stopping the virus from causing a lung infection, and it may also block the cytokine storm that affects seriously ill patients who are hospitalised with COVID-19 however more human studies are needed.	Antihypertensive Anticoagulant Antiviral Antioxidant Anti-inflammatory Anxiolytic Immune Modulator
Perilla *(Perilla frutescens)* 	In a 2021 online assessment study, mast cell activation symptoms were increased in long COVID. It has been postulated that increased activation of abnormal mast cells induced by SARS-CoV-2 infection, by various mechanisms, may underlie part of the cause of long COVID, possibly suggesting routes to effective therapy. Perilla is an antiallergy herb used for histamine intolerance, as seen in hay fever. Preclinical studies indicate that perilla inhibits mast cell-mediated immediate-type allergic reactions. While promising, further study is necessary to determine whether it has these effects in humans.	Anti-inflammatory Antioxidant Antidepressant
Reishi *(Ganoderma lucidum)* 	Reishi is a powerful medicinal mushroom that has been widely used for promoting health and longevity in Asian countries. It is prescribed to enhance immune resistance and prevent opportunistic infections, reducing the risk of continued inflammation and inflammatory response following viral infection. For both of these purposes it is most often combined with other similarly acting immune modulating botanicals such as astragalus and schizandra. Test tube studies have shown that reishi may regulate the inflammation cascade caused by cytokines following a COVID-19 infection, improving the chances of rapid recovery however more studies are needed before this can be extrapolated to human use. Reishi is also used as a general tonic for deficiency syndromes associated with tiredness and fatigue.	Immune Modulator Adaptogen Antioxidant Anti-inflammatory Antiviral Nervine Relaxant

Herbal Support Could Include: (Cont.)

HERB NAME	DESCRIPTION	ACTIONS
St John's Wort *(Hypericum perforatum)* 	Researchers have suggested that St. John's wort could be tested in clinical trials in COVID-19 patients as a multitasker and well tolerated anti-inflammatory agent. The dosage they suggest takes into account the pharmacokinetics data established for antidepressive St. John's wort therapeutic regimens (900 to 1200 mg/day). They said a similar, or slightly increased, daily dosage could be given to COVID-19 patients (drug interactions should be carefully monitored). The researchers concluded that St. John's wort may prevent inflammatory damage in various cell types and tissues. They said experimental studies have shown that St. John's wort can potently counteract the pro-inflammatory effects of various cytokines and it exerted protective effects in models of acute inflammation. Further clinical trials are needed to confirm this.	Anti-inflammatory Nervine Tonic Antiviral Relaxing Nervine Nervous System Trophorestorative Anxiolytic Antidepressant
Withania *(Withania somnifera)* 	Withania is traditionally used in Ayurveda as a powerful adaptogen to boost energy, reduce stress and strengthen the immune system. Recent trials have demonstrated its efficacy in reducing anxiety, stress, improving muscle strength and reducing fatigue symptoms in patients with chronic conditions. It improves the body's defence against disease by improving the cell-mediated immunity and it also possesses potent antioxidant properties that help protect against cellular damage caused by free radicals. A current double-blind clinical trial, taking place over one year, involves 2000 people living in the United Kingdom with long COVID. Half of the trial participants will take 500mg withania tablets, twice a day, for three months, while another 1000 participants will be given a placebo.	Adaptogen Anxiolytic Nervine Tonic Anti-inflammatory Antioxidant Immune Modulator Cardioprotective

Astragalus
(Astragalus membranaceus)

Conclusion

COVID-19 will remain a challenge for the foreseeable future. It is important to remember that the research into long COVID is still in its infancy and the understanding of it, along with COVID-19, continues to evolve. The global definition of long COVID will probably change as new evidence emerges. Researchers are working with patients who develop long COVID to better understand more about its cause, symptoms and effects. The persistent symptoms associated with COVID-19 are frustrating for patients who just want to return to their previous level of function before they had the infection. Unfortunately, there are no clear answers for them at this time. Despite this a clue may be found in the 2021 book *Functional Herbal Therapy* which says that "the take home lesson of the COVID-19 pandemic and its sequelae is that true resilience is fundamentally underpinned by robust health." The book also shines a light on the cardinal lesson from the COVID-19 pandemic that has been neglected by official health care systems, and it seems fitting as a closing remark on long COVID because it gives astounding credence to the naturopathic approach with its focus on overall health, wellness and disease prevention.

"[The COVID-19 pandemic] demonstrates that we have a piecemeal system of "disease care" that leaves us exposed and vulnerable to a novel infectious threat and then struggles to find ways out of the conundrum, still clinging to the "pill (or jab) for every ill" paradigm. COVID-19 forces us to confront the most brutally honest and vitally important question: that we are, on the whole, a sick species, with overall resilience and immune systems that are badly compromised by our modern way of life. It reveals that governments are prepared to spend trillions of dollars on social, economic, and medical remediation of the impact of a virus, but all after the fact. It demonstrates the inherent complacency and short-sightedness of a system of health care that pays only token attention to – and expenditure on – disease prevention and improving community health, and will no doubt continue to do so, despite the now glaring, ultimately costly, deficiencies in this approach."

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