I-RECOVER℠

POST-VACCINE TREATMENT

AN APPROACH TO THE MANAGEMENT OF POST-VACCINE SYNDROME

July 13, 2022

(Changes include: Additional information on autophagy; Added spermidine and resveratrol to first line therapies; Quercetin moved to second line therapy; Fluvoxamine dosing clarified; added Intravenous immunoglobulin (IVIG) treatment and Immunosuppresive therapies to Other Potential Treatments.)

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Disclaimer

This document is primarily intended to assist healthcare professionals in providing appropriate medical care for vaccine-injured patients. Patients should always consult a trusted healthcare provider before embarking on any new treatment.

Contributors

This protocol was a collaborative effort drawing on the expertise of a dozen world-renowned physicians. Dr. Pierre Kory and Dr. Paul Marik are thankful for the contributions of: Dr. Keith Berkowitz; Dr. Flavio Cadegiani; Dr. Suzanne Gazda; Dr. Meryl Nass; Dr. Tina Peers; Dr. Robin Rose; Dr. Yusuf (JP) Saleeby; Dr. Eugene Shippen; Dr. Mobeen Syed; and Dr. Fred Wagshul.

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Definition

Although no official definition exists for 'post-COVID-vaccine syndrome,' a temporal correlation between receiving a COVID-19 vaccine and beginning or worsening of a patient's clinical manifestations is sufficient to diagnose as a COVID-19 vaccine-induced injury when the symptoms are unexplained by other concurrent causes.

Since Phase 3 and Phase 4 clinical trials are still ongoing, the full safety and toxicity profile for COVID-19 vaccines cannot be fully determined. From a bioethical perspective, cases of any new-onset or worsened signs, symptoms or abnormalities following any dose of COVID-19 vaccine must be considered as an injury caused by the vaccine, until proven otherwise.

Note that there are significant overlaps between the symptoms and features of long COVID/long-hauler syndrome and post-vaccine syndrome. However, a number of clinical features appear to be characteristic of post-vaccine syndrome; most notably, severe neurological symptoms appear to be more common following vaccination. To complicate matters further, patients with long COVID are often also vaccinated, making the issue of definition more difficult.

Epidemiology

The Centers for Disease Control (CDC), National Institutes for Health (NIH), Food and Drug Administration (FDA) and World Health Organization (WHO) do not recognize post-vaccine injuries and there is no specific ICD classification code for this disease. Thus, the accurate prevalence of post-vaccine syndrome is unknown. [1]

However, as of July 1, 2022, 839,297 adverse events have been reported in the United States alone following COVID-19 vaccination. This includes 165,088 doctor's office visits, 101,033 urgent care visits, 64,930 hospitalizations, 13,547 deaths, and 12,851 life-threatening events, according to OPEN VAERS, which tracks data recorded in the U.S. Vaccine Adverse Event Reporting System (VAERS). Note that VAERS data is limited by underreporting, by a factor of at least 30-fold. [2] The database also reports 32,068 severe allergic reactions, 14,352 permanent disabilities and 5,724 heart attacks.

The true incidence of adverse events following COVID-19 injections, including deaths and serious vaccine injuries, is unknown. It is likely this data will be hidden and never accurately reported. Published trials

data suggest at least 1.5% to 2% of vaccinated patients develop serious adverse events following vaccination. [2;3] However, a survey by Pollfish released on July 4, 2022 reported that 8.64% of adult respondents who had received a COVID-19 vaccine in the U.S. developed a vaccine injury; translated to the U.S. vaccinated population, this would mean approximately 15 million vaccine injuries. In a similar vein, in a nationwide cohort of U.S. veterans an adverse reaction was reported in 8.5% of recipients of the Pfizer vaccine and 7.9% of those receiving the Moderna vaccine. [4]

As the mainstream medical community does not recognize this serious humanitarian disaster, these patients have been shunned and denied access to the care they need and deserve. Furthermore, there is limited clinical, molecular, and pathological data on these patients to inform an approach to treating the condition. Consequently, our approach to the management of vaccine-injured patients is based on the presumed pathogenetic mechanism, pharmacologic principles, as well as the clinical observations of physicians and patients themselves.

Pathogenesis

The spike protein, notably the S1 segment, is likely the major pathogenetic factor leading to post-vaccine syndrome. [5;6] The S1 protein is profoundly toxic. Multiple intersecting and overlapping pathophysiologic processes likely contribute to the vast spectrum of vaccine injuries: [1;7]

- The acute, immediate reaction (within minutes to hours) is likely the result of an acute type I IgE mediated hypersensitivity reaction. The type I response may be due to preformed antibodies against mRNA, polyethylene glycol (PEG) [8;9] or other components of the nano-lipid particle. In addition, PEG activates multiple 'complement components,' the activation of which may be responsible for both anaphylaxis and cardiovascular collapse. [9-11] A prospective study on 64,900 medical employees, in which reactions to their first mRNA vaccination were carefully monitored, found that 2.1% of subjects reported acute allergic reactions. [12]
- The acute myocarditis/sudden cardiac death syndrome that occurs post vaccination (within hours to 48 hours), noted particularly in young athletes, may be caused by a "stress cardiomyopathy" due to excessive catecholamines produced by the adrenal medulla in response to spike protein-induced metabolic aberrations. [13]
- The subacute and chronic myocarditis is likely the result of a spike protein-induced inflammatory response mediated by pericytes and macrophages. [14;15]
- The subacute (days) and chronic (weeks to years) vaccine-related injuries likely result from the overlapping effects of an S1-induced inflammatory response, the production of autoantibodies, activation of the clotting cascade, and secondary viral reactivation.
- The inflammatory response is mediated by spike protein-induced mononuclear cell activation in almost every organ in the body but most notably involving the brain, heart and endocrine organs.
- Patients with long COVID and those post-vaccination may have spike protein circulating in the blood for as long as 15 months. [16-18] Spike protein inhibits natural killer (NK) cell activity, [19-22] cytotoxic T-cells, and inhibits autophagy; [23] this may account for the persistence of the spike protein.
- The lipid nanoparticles (LNP) themselves are highly proinflammatory, as evidenced by excessive neutrophil infiltration, activation of diverse inflammatory pathways, and production of various inflammatory cytokines and chemokines. [24-26]

- Neuro-COVID, the neurological manifestations related to the spike protein, are related to the complex interplay of neuroinflammation, [27] production of amyloid and prion protein, [28-34] autoantibodies, microvascular thrombosis, and mitochondrial dysfunction. [35]

The spike protein of SARS-CoV-2 has extensive sequence homology with multiple endogenous human proteins and could prime the immune system toward development of both auto-inflammatory and autoimmune disease. [11] As a consequence of molecular mimicry with the spike protein, a diverse spectrum of autoantibodies have been reported. [36-46] These autoantibodies are the likely cause of Guillain-Barré Syndrome (GBS), transverse myelitis, immune thrombocytopenia, and Small Fiber Neuropathy (SFN)/Autonomic neuropathy. [47-54]

Many of these antibodies are directed against G-protein coupled cell membrane receptors. [43;45] Anti-neuronal antibodies likely contribute to the myriad of neurological findings. SFN/autonomic neuropathy appears to be a characteristic disorder following vaccination and is strongly associated with a vast array of autoantibodies. Further, autoantibodies may result in a number of specific syndromes, including anti-phospholipid syndrome, systemic lupus erythematosus (SLE), rheumatoid arthritis, etc.

The spike protein is highly thrombogenic, directly activating the clotting cascade; in addition, the clotting pathway is initiated via inflammatory mediators produced by mononuclear cells and platelets. [6] Activation of the clotting cascade leads to both large clots (causing strokes and pulmonary emboli) as well as microclots (causing microinfarcts in many organs, but most notably the brain). Emerging data suggests that the vaccines can induce an allergic diathesis (eczema, skin rashes, asthma, skin and eye itching, food allergies etc.) This appears to be due to a unique immune dysregulation with antibody class switching (by B cells) and the production of IgE antibodies. There is an overlap with Mast Cell Activation Syndrome (MCAS) and the distinction between the two disorders is not clear. [55;56] However, by definition MCAS has no identifiable causes, is not caused by allergen specific IgE and has no detectable clonal expansion of mast cells. [55]

And finally, due to altered immune function, the activation of dormant viruses and bacterial pathogens may occur, resulting in reactivated Herpes Simplex, Herpes Zoster, Epstein Barr Virus (EBV) and cytomegalovirus (CMV) infection, as well as reactivation of Lyme disease and mycoplasma. [57-60]

The common factor underlying the pathogenic mechanism in the vaccine-injured patient is “immune dysregulation.” The development of immune dysfunction and the severity of dysfunction likely result from a number of intersecting factors, including:

- **Genetics**: First degree relatives of patients who have suffered a vaccine injury appear to be at a very high risk of vaccine injury. Those patients with a methylenetetrahydrofolate reductase (MTHFR) gene mutation [61] and those with Ehlers-Danlos type syndromes may be at an increased risk of injury. MTHFR C677T polymorphism is the most common MTHFR single nucleotide polymorphism (SNP) and the most common genetic cause of hyper-homocysteinemia.[62] Increased homocysteine levels have been linked to worse outcomes in patients with COVID-19. [63;64] Increased homocysteine levels may potentiate the microvascular injury and thrombotic complications associated with the “spikopathy”. [62;65]
- **mRNA load and quantity of spike protein produced**: This may be linked to specific vaccine lots that contain a higher concentration of mRNA. [1] The Moderna vaccine is reported to contain 100 ug of mRNA as compared to 30 ug mRNA for the Pfizer vaccine (10 ug in children 5-11 years age), however, it is likely that the true concentration varies widely.
- **Sex**: It appears that about 80% of vaccine-injured patients are female. Furthermore, treatment with estrogens has been reported to worsen or precipitate an event/relapse. Women are known

to be at a much higher risk of autoimmune diseases (especially SLE) and this likely explains this finding. Estrogens interfere with glucocorticoid receptor signaling. [66] In addition, estrogens modulate B and T cell function.

- **Underlying nutritional status and comorbidities**: It is likely that certain preexisting conditions may have primed the immune system to be more reactive after vaccination. This includes those with preexisting autoimmune disorders and chronic inflammatory diseases such as Lyme disease. Those patients with a poor nutritional status including those with deficiencies of nutrients such as Vitamin D, Vitamin B12, folate and magnesium may be at an increased risk of injury.

Complications/ injuries caused by COVID injections

Over 1,700 peer-reviewed articles have been published on COVID vaccine injuries. Find links to these studies at COVID Vaccine Injuries, REACT19, and on Substack. A selection of symptoms is listed below:

- Myocarditis, pericarditis, stress cardiomyopathy (contraction band necrosis)
- Takotsubo cardiomyopathy
- Acute coronary syndrome
- Hypertension
- MIS-V, Multisystem Inflammatory Syndrome
- Thrombosis, including pulmonary emboli and stroke (prothrombotic state)
- Cerebral venous thrombosis
- Thrombocytopenia
- Thrombotic thrombocytopenic purpura
- Idiopathic thrombocytopenic purpura
- Henoch Schönlein Purpura
- Immune mediated hemolysis
- Menstrual irregularities
- Menorrhagia
- Amenorrhea
- Spontaneous abortion
- Vulval and vaginal ulcers
- Vasculitis, including Leukocytoclastic vasculitis, Granulomatous vasculitis, microscopic polyangiitis
- Guillain-Barre Syndrome
- Acute Myelitis
- Systemic lupus erythematosus
- Bell's Palsy

- Stills disease
- Sweets syndrome
- Facial nerve palsy
- Multiple sclerosis
- Polyarthralgia/polyarthritis
- Cryoglobulinemia
- Lymphadenopathy, local and generalized
- Anaphylaxis
- Allergic reactions
- Intracerebral hemorrhage
- Strokes (thrombotic strokes)
- Generalized neurological symptoms including “brain fog”, cognitive decline, memory loss
- Alzheimer’s Disease like syndrome
- Acute hyperactive encephalopathy
- Acute disseminated encephalomyelitis
- Neuromyelitis Optica
- Ageusia and anosmia
- Aphasia
- Depression
- New onset panic disorders
- New onset psychosis and delirium
- Small fiber neuropathy
- Autonomic neuropathy
- POTS syndrome (postural Orthostatic Tachycardia syndrome)
- Mononeuritis multiplex, polyneuropathy
- Acute inflammatory neuropathies
- Tinnitus (severe and persistent)
- Sensorineural hearing loss
- Vestibulitis
- Severe headaches and migraines
- Seizures and status epilepticus
- Prion disease i.e., Mad Cow Disease

- Acute macular retinopathy
- Uveitis
- Acute Optic Neuropathy
- Rhabdomyolysis
- Keratolysis
- Herpes Keratitis
- Inflammatory myositis
- Immune mediate hepatitis
- Pancreatitis
- Acute kidney injury
- Nephrotic syndrome
- ANCA glomerulonephritis
- Skin reactions including rashes, urticaria, Pityriasis rosea
- Pemphigus vulgaris
- Hemorrhagic bullous pyoderma gangrenosum
- Eosinophilic dermatosis
- Alopecia, including alopecia areata
- Psoriasis
- Toxic epidermal necrolysis
- Erythema multiforme
- Hemophagocytic histiocytosis
- Varicella Zoster infection
- Epstein-Barr viral reactivation
- Herpes Simplex reactivation
- Zoster meningitis
- Ramsay Hunt syndrome
- Thyroiditis
- Tolosa-Hunt syndrome
- Acute eosinophilic pneumonia
- Cancer recurrences
- New and unusual malignancies, including Angioimmunoblastic T Cell Lymphoma

Treatment Approach

A number of principles are essential for the optimal management of post-vaccine syndrome:

- It is important to emphasize that there are no published reports detailing the management of vaccine-injured patients. Our treatment approach is, therefore, based on the postulated pathogenetic mechanism, clinical observation, and patient anecdotes.
- The core problem in post-vaccine syndrome 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.
- Treatment must be individualized according to each patient's presenting symptoms and disease syndromes. It is likely that not all patients will respond equally to the same intervention; this suggests that the treatment must be individualized according to each patient's specific response. A peculiar finding is that a particular intervention (e.g., Hyperbaric oxygen therapy) may be lifesaving for one patient and totally ineffective for another.
- Patients should serve as their own controls and the response to treatment should dictate the modification of the treatment plan.
- Early treatment is essential; it is likely that the response to treatment will 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.
- Patients with post-vaccine syndrome must not receive further COVID-19 vaccines of any type. Likewise, patients with long COVID should avoid all COVID vaccinations.
- Patients with post-vaccine syndrome should do whatever they can to prevent themselves from getting COVID-19. This may include a preventative protocol (see FLCCC protocols). In the event they do contract the virus or suspect infection, early treatment is essential (see FLCCC protocols). It is likely that COVID-19 will exacerbate the symptoms of vaccine injury.
- Vaccine-injured patients are frequently desperate to try any medication or intervention they believe may help them. Unfortunately, unscrupulous providers will take advantage of these very vulnerable patients and sell them expensive and unproven remedies.
- Patients should avoid unscientific and poorly validated "Spike Protein Detox" programs.
- Hyperbaric oxygen therapy (HBOT) should be considered in cases of severe neurological injury and in patients showing a rapid downhill course (see below).

Baseline Testing

Post-vaccine patients are often subjected to an extensive battery of diagnostic tests. These tests are rarely helpful, usually confusing the situation and leading to inappropriate therapeutic interventions. Patients frequently undergo diagnostic tests that are "experimental," unvalidated and clinically meaningless; patients should avoid getting such tests. **Remember the dictum: Only do a test if the result will change your treatment plan.** We recommend a number of simple, basic screening tests that should be repeated, as clinically indicated, every 4 to 6 months.

- CBC with differential and platelet count
- Standard blood chemistries, including liver function tests
- D-Dimer—as a marker of clotting activation. Those with a markedly elevated D-dimer should probably undergo screening for an inherited thrombophilia.
- CRP—as a marker of ongoing inflammation (A comprehensive extensive cytokine/chemokine panel is unnecessary and very costly, and the results will not change the treatment approach.)
- Early morning cortisol—some patients develop autoimmune adrenal failure)
- TSH—to exclude thyroid disease
- Homocysteine level (normal 5-15 µmol/l)
- HbA1C—Vaccine-injured patients are at an increased risk of developing diabetes
- Troponin and pro-BNP to exclude cardiac disease.
- CMV, EBV (early antigen-D IgG or nuclear antigen IgG), Herpes simplex, HHV6 and mycoplasma serology/PCR—to exclude viral/bacterial reactivation (In patients who respond poorly to therapy, it may be helpful to check for Lyme (Bb), Bartonella and Babesia tick-borne diseases—e.g., https://igenex.com/ and https://www.mdlab.com/). [60]
- Vitamin D level (25OH Vitamin D)
- In patients with allergic features and 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. [55]
- In patients who present with dep venous thrombosis (DVT and/or pulmonary embolism soon after vaccination screening for an inherited thrombophilia is suggested. [67]
- Limited screening autoantibodies. Lupus anticoagulant (if positive B2 microglobulin etc.) and ANA. Vaccine-injured patients, particularly those with autonomic dysfunction/SFN frequently have an extensive array of autoantibodies directed against G-protein coupled cell surface receptors, [43;45] ACE-2, [68] neurons, myelin, and other self-epitopes. The presence or absence of these antibodies has little impact on the management of these patients.

First Line Therapies

(not symptom specific; listed in order of importance)

> *"A little starvation can really do more for the average sick man than can the best medicines and the best doctors."*
>
> *—Mark Twain (1835-1910)*

- **Intermittent daily fasting** or periodic daily fasts. Fasting has a profound effect on promoting immune system homeostasis, partly by stimulating the clearing of damaged cells (autophagy), damaged mitochondria (mitophagy) and misfolded and foreign proteins. Fasting also improves mitochondrial health and increases stem cell production. [69-75] Autophagy plays an important role in preventing Alzheimer's disease by removing amyloid protein. It is likely that autophagy 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 injections.

  Note that fasting is contraindicated in patients younger than 18 (impairs growth) and during pregnancy and breastfeeding. Patients with diabetes, as well as those with serious underlying medical conditions, should consult their primary care physician prior to undertaking fasting, as changes in their medications may be required and these patients require close monitoring. Proton pump inhibitors (PPI) should be avoided as they prevent acidification of lysosomes and block autophagy. [76] Chloroquine and hydroxychloroquine (HCQ) act by alkalinizing lysosomes and therefore interfere with the autophagy process. [77] Indeed, high doses of HCQ (more than 800 mg/day) have been demonstrated to improve the outcome of patients with certain cancers by inhibiting autophagy. [78-82] Based on this data, HCQ may limit the benefit of intermittent fasting.

  A number of intermittent fasting plans can be adapted and modified to best suit the patient's lifestyle. [69] For timed fasting, begin slowly: start with an 11-hour eating window 5 days a week and reduce weekly to an 8-hour eating window 7 days a week. This eating window can be shortened to 4 hours or less over time. Timed fasting can be interspersed with 36- to 48-hour fasts. For caloric fasting, eat normally for 5 days and fast for 2 days by restricting caloric intake on those days to 500-1000 calories per day.

- **Spermidine (follow instructions on product) and/or Resveratrol (500 mg twice daily).** Four compunds have been demonstrated to augment autophagy: namely Spermidine, Resveratrol, ivermectin and the diabetic medication metformin. [77;83-94] Spermidine **i**s a naturally occurring polyamine, while resveratrol is a naturally occuring phytochemical. Increased intake of spermidine and resveratrol has been shown to reduce cardiovasular disease, reduce all-cause mortality and prolong lifespan. Spermidine and resveratrol promote autophagy by acting via different metabolic pathways and are therefore likely to have additive or synergistic effects. [91] Furthermore, it is likely that both spermidine and resveratrol potentiate autophagy induced by intermittent fasting. It should be noted that resveratrol binds to the spike protein and this may augment the ability of this molecule to remove the spike protein. [95;96] Wheatgerm, mushrooms, grapefruit, apples and mango are high natural sources of spermidine. [97] Wheatgerm supplements contain high amounts of spermidine. Generally, the oral bioavailability of resveratrol is poor. [98] However, a bioenhanced formulation containing trans-resveratrol from Japanese Knotwood Root appears to have improved bioavailability.

- **Ivermectin; 0.2-0.3 mg/kg, daily for up to 4-6 weeks**. Ivermectin has potent anti-inflammatory properties. [99-101] It also binds to the spike protein, aiding in the elimination by the host. [102-104] It is likely that ivermectin and intermittent fasting act synergistically to rid the body of the spike protein. Ivermectin is best taken with or just following a meal for greater absorption. A trial of ivermectin should be considered as first line therapy. It appears that vaccine-injured patients can be grouped into two categories: i) ivermectin responders and ii) ivermectin non-responders. This distinction is important, as the latter are more difficult to treat and require more aggressive therapy. **Due to the possible drug interaction between quercetin and ivermectin, these drugs should not be taken simultaneously (i.e., should be staggered morning and night).** The safety of ivermectin in pregnancy is uncertain and this drug should be avoided in the first trimeter of pregnancy. [105]
- **Low dose naltrexone (LDN);** LDN has been demonstrated to have anti-inflammatory, analgesic and neuromodulating properties. [106;107] Begin with 1 mg/day and increase to 4.5 mg/day, as required. May take 2 to 3 months to see full effect.
- **Melatonin;** 2-6 mg *slow release/extended release* prior to bedtime. Melatonin has anti-inflammatory and antioxidant properties and is a powerful regulator of mitochondrial function. [108-112] The dose should be started at 750 mcg (μg) to 1 mg at night and increased as tolerated. Patients who are slow metabolizers may have very unpleasant and vivid dreams with higher doses.
- **Aspirin;** 81 mg/day.
- **Vitamin C;** 1000 mg orally two to three times a day. Vitamin C has important anti-inflammatory, antioxidant, and immune-enhancing properties, including increased synthesis of type I interferons. [113-117] Avoid in patients with a history of kidney stones. Oral Vitamin C helps promote growth of protective bacterial populations in the microbiome.
- **Vitamin D** and **Vitamin K2**; The dose of Vitamin D should be adjusted according to the baseline Vitamin D level. However, a dose of 4000-5000 units/day of Vitamin D, together with Vitamin K2 100 mcg/day is a reasonable starting dose.
- ***Nigella sativa* encapsulated oil;** 200-500 mg twice daily. [118-121] It should be noted that thymoquinone (the active ingredient of *Nigella sativa*) decreases the absorption of cyclosporine and phenytoin. Patients taking these drugs should, therefore, avoid taking *Nigella sativa*. [122] Furthermore, two cases of serotonin syndrome have been reported in patients taking *Nigella sativa* who underwent general anesthesia (probable interaction with opiates). [123]
- **Probiotics/prebiotics**; Patients with post-vaccine syndrome classically have a severe dysbiosis with loss of Bifidobacterium. [124-126] Kefir is a highly recommended nutritional supplement high in probiotics. [127] Suggested probiotics include Megasporebiotic (Microbiome labs), TrueBifidoPro (US Enzymes) and yourgutplus+. [128]
- **Magnesium**; 500 mg/day.
- **Omega-3 fatty acids**: Vascepa, Lovaza or DHA/EPA; 4 g/day. Omega-3 fatty acids play an important role in the resolution of inflammation by inducing resolvin production. [129;130]

Patients with elevated homocysteine levels

Patients with elevated homocysteine levels may benefit from treatment with 800 ug of 5-methyl tetrahydrofolate (5-MTHF), the most biologically active form of folic acid. [131] Supplementation with folic acid alone will paradoxically increase homocysteine levels, particularly in patients with MTHFR polymorphism. [131] In addition, B complex vitamins containing B2 (riboflavin) and Vitamin B6, magnesium and Vitamin D should be added. [62]

Adjunctive/Second Line Therapies

(listed in order of importance)

- **Hydroxychloroquine (HCQ);** 200 mg twice daily for 1-2 weeks, then reduce as tolerated to 200 mg/day. HCQ is the preferred second line agent. HCQ is a potent immunomodulating agent and is considered the drug of choice for systemic lupus erythematosus (SLE), where it has been demonstrated to reduce mortality from this disease. Thus, in patients with positive autoantibodies or where autoimmunity is suspected to be a prominent underlying mechanism, HCQ should be considered earlier. Further, it should be noted that SLE and post-vaccine syndrome have many features in common. HCQ is safe in pregnancy; indeed, this drug has been used to treat preeclampsia. [132-136] With long term usage, the dose should be reduced (100 or 150mg/day) in patients weighing less than 61 kg (135 lbs.).
- **"Mitochondrial energy optimizer"** with pyrroloquinoline quinone, glycophospholipids, CoQ10, NADH and other nutrients (e.g., Life Extension Energy Optimizer, Restorative Solutions Mitochondrial Nutrition PQQ, Researched Nutritionals ATP 360® and ATP Fuel® and Pure Encapsulations Mitochondria-ATP) [137-143]
- **Non-invasive brain stimulation (NIBS),** using transcranial direct current stimulation or transcranial magnetic stimulation, has been demonstrated to improve cognitive function in patients with long COVID as well as other neurological diseases. [109-116] NIBS is painless, extremely safe, and easy to administer. NIBS is a recognized therapy offered by many Physical Medicine and Rehabilitation Centers (e.g., see https://www.hopkinsmedicine.org/physical_medicine_rehabilitation/services/programs/brain-stimulation/treatment.html). Patients may also purchase an FDA-approved device for home use (e.g., https://www.fisherwallace.com)
- **N-acetyl cysteine (NAC)**; 600-1500 mg/day [144-146] NAC is the precursor of reduced glutathione. NAC penetrates cells where it is deacetylated to yield L-cysteine thereby promoting GSH synthesis.[146] Based on a broad range of antioxidant, anti-inflammatory and immune-modulating mechanisms, the oral administration of NAC likely plays an adjuvant role in the treatment of the vaccine injured. Oral Glutathione is poorly absorbed and is therefore not recommended. [147;148]
- **Intravenous Vitamin C;** 25 g weekly, together with oral Vitamin C 1000 mg (1 gram) 2-3 times per day. High dose IV vitamin C is "caustic" to the veins and should be given slowly over 2-4 hours. Furthermore, to assess patient tolerability the initial dose should be between 7.5-15 g. Total daily doses of 8-12 g have been well-tolerated, however chronic high doses have been associated with the development of kidney stones, so the duration of therapy should be limited. [103-108] Wean IV Vitamin C as tolerated.

- **Quercetin**. Quercetin is a plant phytochemical (flavonoid) with broad spectrum anti-inflammatory, antioxidant, antiviral, anticoagulant, and immunomodulatory properties. [149-156] In addition, quercetin inhibits mast cells, [157] and has been demonstrated to reduce neuroinflammation. [158] The major limitation of supplemental quercetin is its poor solubility and low oral absorption. [159] A lecithin-based formulation (Quercetin Phytosome®, Life Extension Bio-Quercetin) and a nanoparticle formulation have shown markedly improved bioavailability.[160;161] Quercetin Phytosome (250-500 mg twice daily) has shown promising results in both the prevention and treatment of symptomatic COVID-19 and may have a role in the vaccine injured. [162;163] **Due to the possible drug interaction between quercetin and ivermectin these drugs should not be taken simultaneously (i.e., should be staggered morning and night).** The use of quercetin has rarely been associated with hypothyroidism. [164] The clinical impact of this association may be limited to those individuals with pre-existent thyroid disease or those with subclinical thyroidism. Quercetin should be used with caution in patients with hypothyroidism and TSH levels should be monitored. The safety of quercetin and flavonoids in pregnancy has not been established and they should probably be avoided
- **Fluvoxamine; 50 mg twice daily:** Start on a low dose of 12.5 mg/day and increase slowly as tolerated.
- **Low dose corticosteroid**; 10-15 mg/day prednisone for 3 weeks. Taper to 10 mg/day and then 5 mg/day, as tolerated.
- **Behavioral modification, mindfulness therapy** [165] **and psychological support** may help improve patients' overall well-being and mental health. [166] Suicide is a real problem in the vaccine-injured patient. Support groups and consultation with mental health professionals are important.
- **Tai Chi and Yoga.** Tai Chi, a health-promoting form of traditional Chinese martial art, has shown to be beneficial for preventing and treating diseases including long COVID. [167;168] Yoga has immunomodulating properties that may be beneficial in vaccine-injured patients. [169] It should be noted that long COVID is characterized by severe post-exertional fatigue and/or worsening of symptoms, therefore patients should be counseled to moderate exertion, increasing slowly only as tolerated. [170]

Third Line Therapies

- **Hyperbaric oxygen therapy** (HBOT) [171-179]; HBOT has potent anti-inflammatory properties, decreasing pro-inflammatory cytokines while increasing IL-10. Furthermore, HBOT polarizes macrophages toward the M2 phenotype and improves mitochondrial function. Surprisingly, it is the increased pressure, rather than the increase in the concentration of dissolved oxygen, that appears to mediate these effects. HBOT is delivered at varying pressures, both with and without oxygen. The addition of oxygen increases the clinical response. Maximal clinical response is achieved via use of high-pressure chambers (typically reaching 2.4 ATM) with 100% oxygen for 60 minutes. If HBOT is delivered using lower pressure chambers (less than 1.5 ATM) without supplemental oxygen, the clinical response, although present, is significantly less such that a higher number of sessions will be needed to reach a clinical plateau. While there is very limited published data on the treatment of long COVID and post-vaccine syndrome, remarkable lifesaving benefits have been reported anecdotally. The duration of treatment should be based on clinical response and continue until the benefit has plateaued. If no benefit is evident

clinically after 10 sessions, then HBOT should be considered a therapeutic failure. This therapy is limited by logistical issues and cost.

- **Low Magnitude Mechanical Stimulation** (LMMS or Whole Body Vibration). Low-magnitude (0.3-0.4G), high-frequency (32-40 Hz) mechanical stimulation has been demonstrated to increase bone density as well as indices of general well-being in patients with a variety of medical disorders. [180] It is postulated that this intervention recruits bone marrow stem cells in addition to having metabolic and immunologic effects. In humans, low-magnitude acceleration is applied through the feet by standing on a platform oscillating at relatively high resonant frequency. These parameters are very safe, painless, and easy to administer. This therapy is offered by Physical Medicine and Rehabilitation Centers, or a device may be purchased for home use https://www.juvent.com/health/) similarly with noninvasive brain stimulation (NIBS).

Other Potential Treatments

(Require further evaluation)

- **Plasmapheresis**. Plasmapheresis improves systemic cytokine levels, coagulopathy, and immune responsiveness in patients with severe COVID with a potential mortality benefit. [181-188] Kiprov, et. al. have published a case report of a dramatic clinical improvement in a patient with long COVID. [189] In this report, the patient's markers of inflammatory macrophages diminished and markers of lymphocytes, including natural killer cells and cytotoxic CD8 T-cells, increased; in addition, circulating inflammatory proteins diminished. Furthermore, it is likely that plasmapheresis removes autoantibodies and improves the coagulopathy of these patients. We are aware of anecdotal reports of marked improvement in neurological symptoms, especially SFN and brain fog in vaccine-injured patients treated with this therapeutic modality. However, this is a limited and expensive resource that, in itself, is not without complications. Furthermore, the durability of the clinical response needs to be determined. While plasmapheresis/plasma-exchange is a therapeutic option for the severely neurologically impaired patient following vaccination, additional data is required before this modality can be widely recommended.
- **Pentoxifylline** (PTX); PTX ER, 400 mg three times daily, should be considered in those patients with severe microcirculatory disturbances. PTX is a non-selective phosphodiesterase drug that has anti-inflammatory and antioxidant effects. [190] In addition, PTX improves red blood cell deformability and reduces blood viscosity, so can mitigate the hyper-viscosity and RBCs hyper-aggregation, which is linked with the development of coagulopathy in the vaccine-injured.
- **Maraviroc;** 300 mg orally twice daily. If 6 to 8 weeks have elapsed and significant symptoms persist despite above therapies, this drug can be considered. Note Maraviroc can be expensive and has risk for significant side effects and drug interactions. Maraviroc is a C-C chemokine receptor type 5 (CCR5) antagonist. While many long COVID and post-vaccine patients have been treated with Maraviroc, the role of this drug requires further evaluation. [191]
- **Valproic acid** [192;193]; Depakote, 250mg 2-3 times daily. Valproic acid has anti-inflammatory effects and polarizes macrophages towards a M2 phenotype. [194] HDAC inhibitors are being studied for neural regeneration. In addition, valproic acid has important anticoagulant and anti-platelet effects. [195] Valproic acid may be helpful for neurological symptoms.
- **Sildenafil** with or without L-arginine-L-Citrulline [196-201]; Sildenafil doses titrated up from 25 to 100 mg 2-3 times daily with L-arginine/L-citrulline 5000 mg powder twice daily. May be helpful for brain fog as well as microvascular disease with clotting and poor perfusion. It is

noteworthy that curcumin, resveratrol, EGGG and valproic acid all potentiate phosphodiesterase 5 (PDE5) inhibitors.

- **Sulforaphane (broccoli sprout powder)** 500 mcg – 1g twice a day. While sulforaphane has many potential benefits in patients with COVID, [202-204] long COVID and post-vaccine syndrome, there is limited clinical data to support this intervention. Sulforaphane has immunomodulatory effects by targeting monocytes/macrophages, suggesting a benefit in chronic inflammatory conditions. [202-204] Sulforaphane is a beneficial supplement that may be useful for reducing microglial mediated neuroinflammation and oxidative stress. In addition, as has been well popularized, sulforaphane has an important role in cancer prophylaxis. The pharmacology and optimal dosing of sulforaphane are complex. Sulforaphane itself is unstable. The supplement should contain the two precursors, *glucoraphanin* and *myrosinase*, which react when the supplement is consumed. Broccoli "extracts" are produced in a way that completely destroys the activity of the myrosinase enzyme. As such, these extracts are incapable of producing sulforaphane when consumed in a supplement or food. [205;206] We recommend a 100% whole broccoli sprout powder, which maximally retains both glucoraphanin and myrosinase whilst, at the same time, deactivates the inhibitors.
- **Dandelion** (*Taraxacum officinale*). The root, flower and leaves of dandelion contain an array of phytochemicals that have anti-inflammatory, antioxidant, hypolipidemic, antimicrobial and anticoagulant properties**.** [207;208] It is widely reported that dandelion is effective for 'detoxifying' spike protein. An *in vitro* study demonstrated that a dandelion leaf extract altered the binding of SARS-CoV-2 spike protein to the ACE receptor**.** [209] It would appear that this effect was due to alterations (binding) of the ACE-2 receptor rather than binding to the spike protein. It therefore remains unclear whether dandelion extract actually binds to the spike protein and would potentiate clearance of this protein. The European scientific Cooperative on Phytotherapy recommend a dose of 4-10 g TID (20-30mg/ml in hot water).[210] It should be note that Dandelion extract is considered contraindicated in those with liver and biliary disease, bile duct obstruction, gallstones, cholangitis and active peptic ulcer. [210] Furthermore dandelion is rich in potassium and should be used cautiously in patients with kidney failure.
- **VEDICINALS® 9**; a unique phytopharmaceutical based therapeutic suspension that consists of nine bioactive compounds with antiviral, anti-inflammatory, immune modulatory, anti-pyretic and analgesic properties. The compounds include Baicalin, Quercetin, Luteolin, Rutin, Hesperidin, Curcumin, Epigallocatechin Gallate, Piperine and Glycyrrhizin. (https://www.vedicinals.com/vedicinals-9/). A number of these compounds are included in our protocol and the additional benefit of this 9 phytopharmaceutical combination over more widely available flavanoid combinations is unknown. [211]
- **C60 or C60 fullerenes** [212;213]; C60, short for Carbon 60, is composed of 60 carbon atoms forming something that looks like a hollow soccer ball and considered as a "free radical sponge." C60 is considered the single-most powerful antioxidant ever discovered. Robert Curl, Harold Kroto, and Richard Smalley were awarded the Nobel Prize for chemistry in 1996 for its discovery.
- **Cold Hydrotherapy** (e.g. cold showers) [214;215]; Avoid warm/hot water baths.
- **Intravenous immunoglobulin (IVIG) treatment**; The role of IVIG in the treatment of the vaccine injured is unclear. The response to IVIG in the general population of vaccine-injured patients is mixed, with very few showing long-term improvement. Many patients who report an initial improvement will relapse in 2 to 3 weeks. Other patients report no benefit, while some appear worsened. Due to the presence of non-neutralizing anti-SARS-CoV-2 antibodies and anti-ACE-2

antibodies, etc., the real possibility exists that IVIG will cause antibody dependent immune enhancement (ADE) with a severe exacerbation of symptoms.

IVIG, is however, recommended in specific autoimmune syndromes, which include Guillain Barré Syndrome, transverse myelitis, and immune thrombocytopenia. These patients should concomitantly be treated with the core immune-modulating therapies. IVIG proved to be ineffective in an RCT that enrolled patients with small fiber neuropathy. [299]

The fact that many patients report an initial response to IVIG supports the notion that many aspects of this disease are due to autoantibodies. IVIG will remove preformed antibodies, but they do not prevent the B cells from ongoing antibody production; hence the response is likely to be short-lived and interventions that limit the production of autoantibodies are therefore required (core immune-modulating therapies).

- **Immunosuppressive therapies**; As a rule, immunosuppressive therapy should be avoided, as these drugs may exacerbate the immune dysfunction in vaccine-injured patients and prevent restoration of immune homeostasis. A trial of immunosuppressive therapy may be indicated in patients with an established autoimmune syndrome who have failed other therapeutic interventions.

Disease-Specific Therapeutic Adjuncts

Small fiber neuropathy (SFN)/autonomic neuropathy

- Tricyclic antidepressants (start at low dose and increase as tolerated)
- Gabapentin: 300 mg twice daily and increase as tolerated
- Alpha lipoic acid; 600 mg/day
- POTS – ensure sufficient hydration and consider use of compression stocking or abdominal binders
- POTS – Clonidine; 0.1 mg twice daily as tolerated
- POTS – Fludrocortisone; 0.1 to 0.2 mg/day or licorice root (has glycyrrhizinic acid, an aldosterone-like compound).
- POTS – midodrine; 5-10 mg three times daily
- Whole body vibration therapy has been shown to improve symptoms of small fiber neuropathy. [216;217]
- A trial of hyperbaric oxygen therapy (HBOT)
- Zinc; 25 mg daily (elemental zinc) and together with the zinc ionophore quercetin. SFN is an autoimmune disease; zinc deficiency has been associated with the development of autoimmune diseases. [218]
- It should be noted that the diagnosis of small fiber neuropathy/autonomic neuropathy is a clinical diagnosis. [47-54] Complex and expensive tests are NOT required to make this diagnosis. It should be noted that SFN is closely associated with multiple autoantibodies. Testing for these autoantibodies serves no useful clinical purpose as it does not change the treatment plan.

Generalized neurologic symptoms/"brain fog"/fatigue/visual symptoms

- LDN appears to play a pivotal role in treatment of many neurological symptoms
- Nigella Sativa; 200-500 mg twice daily.
- Intranasal oxytocin. Oxytocin is a nonapeptide produced in the hypothalamus, acting as a neuropeptide in different brain areas (most notably the amygdala and hippocampus) and as a hormone and paracrine substance in peripheral organs.[219;220] Oxytocin has colloquially been referred to as the "love hormone'', given its role in social interaction and bonding.[221] Oxytocin has powerful antiinflammatory and immunomodulating properties and may play an important role in minimizing neuro-inflammation. [184-186] In addition, oxytocin has been demonstrated to stimulate neuronal growth [220] Oxytocin plays an important role in modulating the stress response.[222] Oxytocin has also been reported to have a role in the prevention and treatment of migraine. [223;224] The nasal route appears to be the preferred mode of administration. Martins et al performed a dose finding study in healthy human volunteers. [187] These authors measured changes in amygdala blood flow and demonstrated an inverse dose response curve, with lower doses resulting in a greater increase in blood flow. They report the optimal dose as being between 9-18 IU. This suggest that one to two puffs to each nostril (4 IU per puff) two times a day may be optimal (total dosage of 16-32 IU per day). Oxytocin must be avoided in pregnancy.
- Spermidine and Resveratrol**.** Experimental studies have demonstrated that spermidine reduces neuroinflammation, reduces accumulation of amyloid protein and improves cognitive function.[225;226] Similarly, resveratrol has been shown to be useful in the prevention and treatment of Alzheimer's disease. [87]
- Non-invasive brain stimulation (NIBS) should be considered in patients with "brain fog," memory disturbances and as well as other cognitive issues.
- Valproic acid and pentoxifylline may be of value in these patients.
- Fluvoxamine: Start on a low dose of 12.5 mg/day and increase slowly as tolerated. Some patients report a significant improvement with fluvoxamine while other patients appear to tolerate this drug poorly. Fluoxetine 20 mg/day is an alternative, as are tricyclic anti-depressants (see section on Depression below).
- These symptoms may be mediated by Mast Cell Activation Syndrome (MCAS); see specific treatment below.

Depression

- Depression is a serious problem in long COVID and the post-vaccine patients and, unfortunately, suicide is not uncommon. [227-229] Patients with a history of depression and/or those taking SSRI medications appear to be at particular risk of severe depression.
- Patients with depression are best managed by mental health providers with expertise in this area. Long term SSRI medications are generally not recommended due to the long-term effects of these drugs on serotonin receptors, intracellular messenger pathways as well genetic and epigenetic effects.[230;231] Short term fluvoxamine may have a role in these patients. It should be note that most SSRI/SNRI agents, but notably sertraline, paroxetine, venlafaxine, and duloxetine are

associated with self-inflicted harm, suicide, anger outbursts, physical violence, homicidal thoughts and homicide. [232-234] Patients who are treated with antidepressant agents therefore require close monitoring for the development of these serious adverse reactions.

- There appears to be an interaction between vaccination, COVID-19, zinc levels and depression. [235-238] COVID-19 infection and COVID vaccines may lead to low zinc levels. Zinc deficiency is associated with an increased risk of depression. Treatment with zinc has been shown to have antidepressant effects and to act synergistically with SSRI medication. [239] 25 mg zinc daily (elemental), together with the zinc ionophore quercetin is therefore suggested. [238]
- Non-invasive brain stimulation (NIBS) using transcranial direct current stimulation or transcranial magnetic stimulation has been demonstrated to be highly effective in the treatment of depression. [240-244] Indeed, The Fisher Wallace Stimulator® is FDA approved for the treatment of depression, anxiety, and insomnia. NIBS is painless, extremely safe, and easy to administer. NIBS is a recognized therapy offered by many Physical Medicine and Rehabilitation Centers. Patients may also purchase an FDA-approved device for home use (https://www.fisherwallace.com/).
- In experimental models, *Nigella sativa* has been shown to have a role in the treatment of depression. [169]
- Altered gut flora (microbiome) has been linked to anxiety and depression. [170-172] Since the vaccines have been demonstrated to alter the microbiome, the use of probiotics is suggested. [74-76] Kefir is a highly recommended nutritional supplement high in probiotics. [77] Suggested probiotics include Megasporebiotic (Microbiome labs) and TrueBifidoPro (US Enzymes) and yourgutplus+. [128]

Patients with elevated DIC and those with evidence of thrombosis

- These patients should be treated with a NOAC or coumadin for at least three months and then reevaluated for ongoing anticoagulation.
- Patients should continue ASA 81 mg/day unless at high risk of bleeding.
- Lumbrokinase activates plasmin and degrades fibrin. e.g., Lumbroxym (US Enzymes). [245] Lumbrokinase appears to be well absorbed from the GI tract. [246]
- Turmeric (Curcumin) 500 mg twice a day. Curcumin has anticoagulant, antiplatelet and fibrinolytic properties. [247] [248;249] Curcumin has low solubility in water and is poorly absorbed by the body; [250] consequently, it is traditionally taken with full fat milk and black pepper, which enhance its absorption. Nano-curcumin preparations or formulations designed to enhance absorption are encouraged.[251-254]
- Triple anticoagulation should be considered in select patients. [255] Treat no longer than one month. Triple anticoagulation increases the risk of serious bleeding; patients should be counseled regarding this complication.
- In those patients with marked microvascular disease/thrombosis, the combination of pentoxifylline and sildenafil should be given a therapeutic trial. [190;256]

Vaccine induced myocarditis/pericarditis

- ACE inhibitor/ARB, together with carvedilol as tolerated to prevent/limit progressive decline in cardiac function.

- Colchicine in patients with pericarditis – 0.6 mg/day orally; increase to 0.6 mg twice daily if required. Reduce dose if patients develop diarrhea. Monitor white blood cell count. Decrease dose with renal impairment.
- Referral to a cardiologist or ER in case of persistent chest pain or other signs and symptoms of cardiac events are observed.

Herpes virus reactivation syndrome

- Valtrex; 500-1000 mg twice daily for 7-10 days (acyclovir is an alternative). [257]
- Spironolactone 50-100 mg daily [258]. Spironolactone has antiviral properties against Epstein Barr Virus by inhibiting viral capsid antigen synthesis and capsid formation. Spironolactone likely has antiviral effects against other Herpes viruses.
- L-Lysine; 1000 mg twice daily [259;260]
- Valproic acid; Depakote, 250 mg 2-3 times daily. Valproic acid has activity against HSV-1, HSV-2, HZV, CMV and EBV. [261-263]
- Zinc 40 mg daily [264;265]
- Quercetin "Phytosome" 500 mg twice daily (antiviral properties and a Zinc ionophore) [266]

Tinnitus

- This a frequent and disabling complication reported in post-vaccine syndrome.
- Tinnitus refers to the sensation of sound in the absence of a corresponding external acoustic stimulus and can, therefore, be classified as a phantom phenomenon. Tinnitus sensations are usually of an unformed acoustic nature such as buzzing, hissing, or ringing. Tinnitus can be localized unilaterally or bilaterally, but it can also be described to emerge within the head. [267]
- Ideally, patients should be evaluated by an ENT specialist or audiologist to exclude underlying disorders.
- A number of treatment approaches exist to manage this disabling disease including: [267-269]
    - Cognitive behavioral therapy [270]
    - Specialized therapy including tinnitus retraining therapy, hearing aids, sound therapy, auditory perceptual training and repetitive transcranial magnetic stimulation. [267]
    - A number of pharmacologic agents have been used to treat tinnitus. Anticonvulsants including carbamazepine have generally been disappointing. The following drugs have shown some clinical benefit.
        - Tricyclic antidepressant agents particularly nortriptyline and amitriptyline. [271;272] In addition, the SSRI sertraline has shown some efficacy. [273]
        - Clonazepam and or other benzodiazepines. These drugs may provide temporary relief, however, due to issue of dependence, long term use is not recommended. [274]
        - Melatonin slow release 2-6 mg at bedtime. [275]
- Oxytocin nasal spray. Oxytoxin acts as a neurotransmitter affecting a number of neural circuits particularly in the hypothalamus and amygdala. Oxytocin nasal spray has shown promising

results for the treatment of tinnitus (one puff to each puff nostril two time a day; a total dosage of 16 IU per day).[276] Oxytocin must be avoided in pregnancy

- Non-invasive brain stimulation (NIBS) has proven to be effective in controlling treatment-resistant tinnitus. [277;278]

Ageusia and anosmia (Loss of taste and smell)

- Loss of smell and taste is a troubling symptom in post-COVID patients and in the vaccine injured. The loss of taste usually follows the loss of smell. Multiple mechanism may explain the loss of smell including direct injury to the olfactory bulb.[279] Anosmia is a particularly difficult condition to treat. [280]
- Oxytocin nasal spray. Oxytocin receptors are highly expressed on olfactory neurons as well as limbic structures. Oxytocin nasal spray has been demonstrated to improve the sense of smell in patients with schizophrenia. A dose of one puff in each nostril two time a day for a total dosage of 16 IU per day is suggested. [281] Oxytocin must be avoided in pregnancy.
- Olfactory training appears to be a promising therapy for patients with postviral olfactory loss to partly regain their sense of smell. [282]
- Nasal corticosteroids appear ineffective and are not recommend for the use of anosmia. [283]

Bell's palsy/facial paresthesia/visual issues

- Low dose naltrexone. Begin with 1 mg/day and increase to 4.5 mg/day as required. May take 2-3 months for full effect.
- Low dose corticosteroid: 10-15 mg/day prednisone for 3 weeks. Taper to 10 mg/day and then 5 mg/day as tolerated.
- Reduced workload, stress, and light exercises for a couple of months.

Patients with new onset allergic diathesis/features of Mast Cell Activation Syndrome (MCAS)

- The novel flavanoid luteolin is reported to be a potent mast cell inhibitor. [284-287] Luteolin 20-100 mg/day is suggested.
- Turmeric (curcumin); 500 mg/day. Curcumin has been reported to block H1 and H2 receptors and to limit mast cell degranulation. [248;249] Curcumin has low solubility in water and is poorly absorbed by the body; [250] consequently, it is traditionally taken with full fat milk and black pepper, which enhance its absorption. Nano-curcumin preparations or formulations designed to enhance absorption are encouraged. [251-254]
- H1 receptor blockers. Loratadine 10 mg/day, Cetirizine 5-10 mg/day, Fexofenadine 180 mg/day.
- H2 receptor blockers. Famotidine 20 mg twice daily as tolerated. [288]
- Montelukast 10 mg/day. Caution as may cause depression is some patients. The efficacy of montelukast as a "mast cell stabilizer' has been questioned. [55]
- Ketotifen. 1 mg in 5 ml. Start with 0.5 ml at night. Once they get used to it, as it has a strong hypnotic effect, increase by 0.5ml increments up to 5ml. Some patients can increase up to 10 ml daily (1 mg BID). Ketotifen has antihistamine effects and is a mast cell stabilizer. Ketotifen may be particularly useful in patients with GI hypersensitivity.[289;290]

- Vitamin C; 1000 mg twice daily. Vitamin C is strongly recommended for allergic conditions and MCAS. Vitamin C modulates immune cell function and is a potent histamine inhibitor.
- Low histamine diet.

Alopecia (hair loss)

Three types of alopecia have been described in connection with COVID-19 infection, long COVID and post-vaccine syndrome. [291]

- Androgenetic alopecia (worsening of male pattern baldness)
- Alopecia areata, an autoimmune disorder that usually results in unpredictable, patchy hair loss. In most cases, hair falls out in small patches around the size of a quarter. There is currently no cure for alopecia areata; referral to a dermatologist is suggested. Preliminary research in animals has found that quercetin can protect against the progression of alopecia areata and may promote hair regrowth. [292;293]
- Telogen effluvium, which results in temporary thinning of the hair particularly on the scalp. Telogen effluvium is a reversible condition in which hair falls out after a stressful experience. The stress pushes large numbers of hair follicles into a resting phase. Within a few months, those hairs can fall out. This condition occurs predominantly in females and may be related to increased expression of pro-inflammatory mediators. No specific treatment is required, as the hair will usually grow back.
- Nutritional supplements containing omega-3 fatty acids (Vascepa), vitamin D, vitamin C and zinc are useful adjuncts to promote hair regrowth. [294-296]
- Topical minoxidil may promote hair regrowth.[297] Finasteride 2.5 mg daily is an option in both men and women; [298] consult with a dermatologist and treatment for less than 1 year is generally recommended.

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