

I-RECOVERSM

POST-VACCINE TREATMENT

AN APPROACH TO THE MANAGEMENT OF POST-VACCINE SYNDROME

July 3, 2022

(Changes include additional information on pathogenesis; non-invasive brain stimulation and yoga added to second line therapies; whole body vibration therapy added to third line therapies; dandelion added to other potential treatments; details added to depression section on risks related to SSRIs; additional treatments for Herpes virus reactivation syndrome and alopecia.)

Table of Contents

<i>Disclaimer</i>	3
<i>Contributors</i>	3
<i>Definition</i>	3
<i>Epidemiology</i>	3
<i>Pathogenesis</i>	4
<i>Treatment Approach</i>	6
<i>Baseline Testing</i>	7
<i>First Line Therapies</i>	8
<i>Adjunctive/Second Line Therapies</i>	9
<i>Third Line Therapies</i>	11
<i>Other Potential Treatments</i>	11
<i>Disease-Specific Therapeutic Adjuncts</i>	13
Small fiber neuropathy (SFN)/autonomic neuropathy.....	13
Generalized neurologic symptoms/“brain fog”/fatigue/visual symptoms	14
Depression.....	14
Patients with elevated DIC and those with evidence of thrombosis	15
Vaccine induced myocarditis/pericarditis	15
Herpes virus reactivation syndrome.....	16
Tinnitus	16
Bell’s palsy/facial paresthesia/visual issues	17
Patients with new onset allergic diathesis/features of Mast Cell Activation Syndrome (MCAS).....	17
Alopecia (hair loss)	18
Intravenous immunoglobulin (IVIG) treatment	18
Immunosuppressive therapies	19
<i>References</i>	20

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.

We are also extremely grateful for the feedback of the many vaccine-injured people who shared their experiences with us.

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 May 27, 2022, 825,453 adverse events have been reported in the United States alone following COVID-19 vaccination. This includes 163,283 doctor’s office visits, 100,259 urgent care visits, 63,368 hospitalizations, 13,150 deaths, and 12,746 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 reports 30,717 severe allergic reactions, 14,181 permanent disabilities and 5,888 heart attacks.

Furthermore, published trials data suggest that at least 1 to 1.5 percent of vaccinated patients develop serious adverse events following vaccination. [2;3] Since 572 million doses of a COVID-19 vaccine have been administered in the U.S.—and 11 billion worldwide—it is likely there are millions of vaccine-injured patients worldwide, and at least 2 million cases in the U.S.

As the medical community does not recognize this serious humanitarian disaster, these patients have unfortunately been shunned and denied access to the medical 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, 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. [4;5] The S1 protein is profoundly toxic. Multiple intersecting and overlapping pathophysiologic processes likely contribute to the vast spectrum of vaccine injuries: [1;6]

- 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) [7;8] 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. [8-10] 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. [11]
- 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. [12]
- The subacute and chronic myocarditis is likely the result of a spike protein-induced inflammatory response mediated by pericytes and macrophages. [13;14]
- 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.
- 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. [15-17]
- Neuro-COVID, the neurological manifestations related to the spike protein, are related to the complex interplay of neuroinflammation, [18] production of amyloid and prion protein, [19-25] autoantibodies, microvascular thrombosis, and mitochondrial dysfunction. [26]

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.[10] As a consequence of molecular mimicry with the spike protein, a diverse spectrum of autoantibodies have been reported. [27-37] These autoantibodies are the likely cause of Guillain-Barré Syndrome (GBS), transverse myelitis, immune thrombocytopenia, and Small Fiber Neuropathy (SFN)/Autonomic neuropathy. [38-45]

Many of these antibodies are directed against G-protein coupled cell membrane receptors. [34;36] 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. [5] 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. [46;47] However, by definition MCAS has no identifiable causes, is not caused by allergen specific IgE and has no detectable clonal expansion of mast cells. [46]

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. [48-51] 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 [52] 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.[53] Increased homocysteine levels have been linked to worse outcomes in patients with COVID-19. [54;55] Increased homocysteine levels may potentiate the microvascular injury and thrombotic complications associated with the “spikopathy”. [53;56]
- **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 50 ug mRNA for the Pfizer vaccine, however it is likely that the true concentration varies widely.**
- **Sex:** It appears that about 80 percent 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. [57] 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, Vitamin D, folate and magnesium may be at an increased risk of injury.

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 life-saving 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 umol/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/>). [51]
- 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. [46]
- In patients who present with deep venous thrombosis (DVT and/or pulmonary embolism soon after vaccination screening for an inherited thrombophilia is suggested. [58]
- 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, [34;36] ACE-2, [59] 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)

- **Intermittent daily fasting** or periodic daily fasts; Fasting has a profound effect on promoting immune system homeostasis, partly by stimulating autophagy and clearing misfolded and foreign proteins, promoting mitophagy and improving mitochondrial health, as well as increasing stem cell production. [60-66] Intermittent fasting likely has an important role in promoting the breakdown and elimination of the spike protein. 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. **There are a number of intermittent fasting plans that can be adapted and modified to best suit the patient's lifestyle.**[60] For timed fasting, begin slowly: start with an 11-hour eating window 5 days a week and reduce monthly 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 36–48-hour fasts.** For caloric fasting, eat normally for 5 days and fast for 2 days, restricting caloric intake to 500-1000 kcal per day. Proton pump inhibitors (PPI) should be avoided as they prevent acidification of lysosomes and block autophagy. [67] **Chloroquine and hydroxychloroquine act by alkalinizing lysosomes and therefore interfere with the autophagy process. Indeed, high dose HCQ (≥ 800 mg/day) have been demonstrated to improve the outcome of patients with certain cancers by inhibiting autophagy.**[68-72] Based on this data HCQ may limit the benefit of intermittent fasting.
- **Spermidine** is a naturally occurring polyamine which has been demonstrated to promote autophagy.[73;74] Increased intake of spermidine has been shown to reduce cardiovascular disease, reduce all cause mortality and prolong lifespan.[75-78] It is likely that spermidine potentiates autophagy induced by intermittent fasting. Wheatgerm, mushrooms, grapefruit, apples and mango are high natural sources of spermidine.[76] wheatgerm supplements contain high amounts of spermidine.
- **Ivermectin; 0.2-0.3 mg/kg, daily for up to 4-6 weeks.** Ivermectin has potent anti-inflammatory properties. [79-81] It also binds to the spike protein, aiding in the elimination by the host. [82-84] 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 trimester of pregnancy. [85]
- **Low dose naltrexone (LDN);** LDN has been demonstrated to have anti-inflammatory, analgesic and neuromodulating properties. [86;87] 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.

“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)

[88-92] 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 three to four times a day. Vitamin C has important anti-inflammatory, antioxidant, and immune-enhancing properties, including increased synthesis of type I interferons. [93-97] 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**; 200-500 mg twice daily. [98-101] 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. [102] Furthermore, two cases of serotonin syndrome have been reported in patients taking Nigella Sativa who underwent general anesthesia (probable interaction with opiates). [103]
- **Probiotics/prebiotics**; Patients with post-vaccine syndrome classically have a severe dysbiosis with loss of Bifidobacterium. [104-106] Kefir is a highly recommended nutritional supplement high in probiotics. [107] Suggested probiotics include Megasporebiotic (Microbiome labs), TrueBifidoPro (US Enzymes) and yourgutplus+. [108]
- **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 resolvins production. [109;110]

Treatment of patients with elevated homocysteine levels

Patients with elevated homocysteine levels may benefit from treatment with 800 μg of 5-methyl tetrahydrofolate (5-MTHF), the most biologically active form of folic acid.[111] Supplementation with folic acid alone will paradoxically increase homocysteine levels particularly in patients with MTHFR polymorphism.[111] In addition, B complex vitamins containing B2 (riboflavin) and vitamin B6, magnesium and Vitamin D should be added. [53]

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. [112-116] 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, glycerophospholipids, 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) [117-123]
- **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 [124-126] NAC is the precursor of reduced glutathione. NAC penetrates cells where it is deacetylated to yield L-cysteine thereby promoting GSH synthesis.[126] Based on a broad range of antioxidant, anti-inflammatory and immunomodulating 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. [127;128]
- **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 (flavanoid) with broad spectrum anti-inflammatory, antioxidant, antiviral, anticoagulant, and immunomodulatory properties. [129-136] In addition, quercetin inhibits mast cells,[137] and has been demonstrated to reduce neuroinflammation.[138] The major limitation of supplemental quercetin is its poor solubility and low oral absorption.[139] A lecithin-based formulation (Quercetin Phytosome®, Life Extension Bio-Quercetin) and a nanoparticle formulation have shown markedly improved bioavailability.[140;141] Quercetin Phytosome (250- 500 mg BID) has shown promising results in both the prevention and treatment of symptomatic COVID-19 and may have a role in the vaccine injured. [142;143] 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. [144] 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**; 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 [145] and psychological support** may help improve patients’ overall well-being and mental health. [146] 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. [147;148] Yoga has immunomodulating properties that may be beneficial in vaccine-injured patients. [149] 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. [150]

Third Line Therapies

- **Hyperbaric oxygen therapy (HBOT)** [151-159]; 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. While the optimal dose and dosing schedule is unclear, a pressure of between 1.5 and 2.0 ATM appears to be necessary to mediate the anti-inflammatory effects; however, others have reported improvements with a little as 1.3 ATM. Pressures above 1.3 ATM can only be achieved using hard shell chambers. 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.
- **LMMS - Low Magnitude Mechanical Stimulation (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.[160] 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. [161-168] Kiprof, et. al. have published a case report of a dramatic clinical improvement in a patient with long COVID. [169] 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. [170] 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. [171]
- **Valproic acid** [172;173]; Depakote, 250mg 2-3 times daily. Valproic acid has anti-inflammatory effects and polarizes macrophages towards a M2 phenotype. [174] HDAC inhibitors are being studied for neural regeneration. In addition, valproic acid has important anticoagulant and anti-platelet effects. [175] Valproic acid may be helpful for neurological symptoms.
- **Sildenafil** with or without L-arginine-L-Citrulline [176-181]; 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, [182-184] 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. [182-184] 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. [185;186] 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. [187;188] 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. [189] 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).[190] It should be noted that Dandelion extract is considered contraindicated in those with liver and biliary disease, bile duct obstruction, gallstones, cholangitis and active peptic ulcer. [190] 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. [191]
- **C60 or C60 fullerenes** [192;193]; 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) [194;195]; Avoid warm/hot water baths.

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. [196;197]
- 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. [198]
- It should be noted that the diagnosis of small fiber neuropathy/autonomic neuropathy is a clinical diagnosis. [38-45] 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.[199;200] Oxytocin has colloquially been referred to as the “love hormone”, given its role in social interaction and bonding.[201] 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 [200] Oxytocin plays an important role in modulating the stress response.[202] Oxytocin has also been reported to have a role in the prevention and treatment of migraine. [203;204] 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 is a naturally occurring polyamine which has been demonstrated to promote autophagy.[73;74] Experimental studies have demonstrated that spermidine reduces neuroinflammation, reduces accumulation of amyloid protein and improves cognitive function.[205;206]**
- 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. [207-209] 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.[210;211] 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. [212-214] 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. [215-218] 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. [219] 25 mg zinc daily (elemental), together with the zinc ionophore quercetin is therefore suggested. [218]
- 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. [220-224] 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+. [108]

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). [225] Lumbrokinase appears to be well absorbed from the GI tract. [226]
- Turmeric (Curcumin) 500 mg twice a day. Curcumin has anticoagulant, antiplatelet and fibrinolytic properties. [227] [228;229] Curcumin has low solubility in water and is poorly absorbed by the body; [230] 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.[231-234]
- Triple anticoagulation should be considered in select patients. [235] 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. [170;236]

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). [237]
- Spironolactone 50-100 mg daily [238]. 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 [239;240]
- Valproic acid; Depakote, 250 mg 2-3 times daily. Valproic acid has activity against HSV-1, HSV-2, HZV, CMV and EBV. [241-243]
- Zinc 40 mg daily [244;245]
- Quercetin “Phytosome” 500 mg twice daily (antiviral properties and a Zinc ionophore) [246]

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. [247]
- 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: [247-249]
 - Cognitive behavioral therapy [250]
 - Specialized therapy including tinnitus retraining therapy, hearing aids, sound therapy, auditory perceptual training and repetitive transcranial magnetic stimulation. [247]
 - 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. [251;252] In addition, the SSRI sertraline has shown some efficacy. [253]
 - Clonazepam and or other benzodiazepines. These drugs may provide temporary relief, however, due to issue of dependence, long term use is not recommended. [254]
 - Melatonin slow release 2-6 mg at bedtime. [255]
- Oxytocin nasal spray. Oxytocin 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 nostril two time a day; a total dosage of 16 IU per day).[256] Oxytocin must be avoided in pregnancy
- Non-invasive brain stimulation (NIBS) has proven to be effective in controlling treatment-resistant tinnitus. [257;258]

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.[259] Anosmia is a particularly difficult condition to treat. [260]
- 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. [261] 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.[262]
- Nasal corticosteroids appear ineffective and are not recommend for the use of anosmia.[263]

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. [264-267] 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. [228;229] Curcumin has low solubility in water and is poorly absorbed by the body; [230] 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. [231-234]
- 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. [268]
- Montelukast 10 mg/day. Caution as may cause depression is some patients. The efficacy of montelukast as a "mast cell stabilizer" has been questioned. [46]
- 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.[269;270]
- 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. [271]

- 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. [272;273]
- 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. [274-276]
- Topical minoxidil may promote hair regrowth.[277] Finasteride 2.5 mg daily is an option in both men and women;[278] consult with a dermatologist and treatment for less than 1 year is generally recommended.

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. [279]
- 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.

References

Reference List

1. Blaylock RL. COVID Update: What is the truth? *Surgical Neurology International* 2022; 13.
2. Rose J. A report on the U.S. Vaccine Adverse Events Reporting System (VAERS) of the COVID-19 messenger ribonucleic acid (mRNA) biologicals. *Science, Public Health Policy, and Law* 2021; 2:59-80.
3. Neil M, Fenton N, Smalley J, Craig C, Guetzkow J, Rose J. Latest statistics on England mortality data suggest systematic mis-categorisation of vaccine status and uncertain effectiveness of Covid-19 vaccination. *Research Gate* 2021.
4. Colunga Biancatelli RM, Solopov P, Sharlow E, Lazo J, Marik PE, Catravas J. The SARS-CoV-2 spike protein subunit 1 induces COVID-19 like acute lung injury in K18-hACE2 transgenic mice and barrier dysfunction in human endothelial cells. *Am J Physiol Lung Cell Mol Physiol* 2021; 321:L477-L484.
5. Marik P, Iglesias J, Varon J, Kory P. A Scoping Review of the pathophysiology of COVID-19. *International Journal of Immunopathology and Pharmacology* 2021.
6. Seneff S, Nigh G, Kyriakopoulos AM, McCullough PA. Innate immune suppression by SARS-C-V-2 mRNA vaccinations: The role of G-quadruplexes, exosomes and microRNAs. *Food & Chemical Toxicology* 2022; 164:113008.
7. Chen BM, Cheng TL, Roffler SR. Polyethylene glycol immunogenicity: Theoretical, clinical and practical aspects of anti-polyethylene glycol antibodies. *ASC Nano* 2021; 15:14022-14048.
8. Mohamed M, Lila AS, Shimizu T, Alaaeldin E, Hussein A, Sarhan HA et al. PEGylated liposomes: immunological responses. *Science and Technology of Advanced Materials* 2019; 20:710-724.
9. Hamad I, Hunter AC, Szebeni J, Moghimi SM. Poly (ethylene glycol)s generate complement activation products in human serum through increased alternative pathway turnover and a MASP-2 dependent process. *Molecular Immunology* 2008; 46:225-232.
10. Seneff S, Nigh G. Worse than the disease? Reviewing some possible unintended consequences of the mRNA vaccines against COVID-19. *International Journal of Vaccine Theory, Practice, and Research* 2021; 2:38-79.
11. Blumenthal KG, Robinson LB, Camargo CA, Shenoy ES, Banerji A, Landman AB. Acute allergic reactions to mRNA COVID-19 vaccines. *JAMA* 2022; 325:1562-1564.
12. Cadejani FA. Catecholamines are the key trigger of mRNA SARS-CoV-2 and mRNA COVID-19 vaccine-induced myocarditis and sudden deaths: a compelling hypothesis supported by epidemiological, anatomopathological, molecular and physiological findings. *medRxiv* 2022.

13. Schauer J, Buddhe S, Gulhane A, Sagiv E. Persistent cardiac MRI findings in a cohort of adolescents with post COVID-19 mRNA vaccine myopericarditis. *J Pediatr* 2022.
14. Verma AK, Lavine KJ, Lin CY. Myocarditis after COVID-19 mRNA vaccination. *N Engl J Med* 2022; 385:1332-1334.
15. Verbeke R, Lentacker I, Smedt SC, DeWitte H. Three decades of messenger RNA vaccine development. *Nanotoday* 2019; 28:100766.
16. Parhiz H, Brenner JS, Patel PN, Papp TE, Li Q, Shi R. Added to pre-existing inflammation, mRNA-lipid nanoparticles induce inflammation exacerbations (IE). *Journal of Controlled Release* 2022; 344:50-61.
17. Ndeupen S, Qin Z, Jacobsen S, Bouteau A, Estanbouli H, Igyarto BZ. The mRNA-LNP platform's lipid nanoparticle component used in preclinical vaccine studies is highly inflammatory. *iScience* 2021; 24:103479.
18. Olajide O, Iwuanyanwu VU, Adegbola OD, Al-Hindawi AA. SARS-CoV-2 spike glycoprotein S1 induces neuroinflammation in BV-2 microglia. *Molecular Neurobiology* 2022; 59:45-458.
19. Nystrom S, Hammarstrom P. Amyloidogenesis of SARS-CoV-2 spike protein. *Journal of the American Chemical Society* 2022.
20. Charnley M, Islam S, Bindra G, Ratcliffe J, Zhou J, Hulett M. Neurotoxic amyloidogenic peptides identified in the proteome of SARS-COV-2: potential implications for neurological symptoms in COVID-19. *Nature Communications* 2022; 13:3387.
21. Mohabatkar H, Behbahani M, Moradi M. A concise in silico prediction report of a potential prion-like domain in SARS-CoV-2 polyprotein. *Journal of Microbiology, Biotechnology and Food Sciences* 2021; 11:e4813.
22. Idrees D, Kumar V. SARS-CoV-2 spike protein interactions with amyloidogenic proteins: potential clues to neurodegeneration. *Biochemical and Biophysical Research Communications* 2021; 554:94-98.
23. Classen JB. Review of COVID-19 vaccines and the risk of chronic adverse events including neurological degeneration. *J Med Clin Res Rev* 2021; 5:1-7.
24. Kuyandik A, Ozcan E, Serin S, Sungurtekin H. Creutzfeldt-Jakob disease after COVID-19 vaccination. *Turk J Intensive Care* 2021.
25. Perez JC, Moret-Chalmin C, Montagnier L. Towards the emergence of a new form of the neurodegenerative Creutzfeldt-Jakob disease: Twenty six cases of CJD declared a few days after a COVID-19 "vaccine" jab. *Research Square* 2022.
26. Clough E, Chean KT, Inigo J, Tubbesing KE, Chandra D, Chaves L. Mitochondrial dynamics in SARS-CoV-2 spike protein treated human microglia: Implications for neuro-COVID. *Journal of Neuroimmune Pharmacology* 2022.

27. Schiaffino MT, Di Natale M, Garcia-Martinez E, Navarro J, Munoz-Blanco JL, Demelo-Rodriguez P. Immunoserologic detection and diagnostic relevance of cross-reactive autoantibodies in Coronavirus disease 2019 patients. *J Infect Dis* 2020; 222:1439-1443.
28. Trahtemberg U, Fritzler MJ. COVID-19-associated autoimmunity as a feature of acute respiratory failure. *Intensive Care Med* 2021.
29. Woodruff MC, Ramoneli RP, Lee FE, Sanz I. Broadly-targeted autoreactivity is common in severe SARS-CoV-2 infection. *medRxiv* 2020.
30. Zuo Y, Estes SK, Ali RA, Gandhi AA, Shi H. Prothrombotic autoantibodies in the serum from patients hospitalized with COVID-19. *Sci Translation Med* 2020.
31. Pascolini S, Vannini A, Deleonardi G, Ciordinik M, Sensoli A. COVID-19 and immunological dysregulation: can autoantibodies be useful? *Clin Trans Sci* 2021; 14:502-508.
32. Wang EY, Mao T, Klein J, Dai Y, Huck JD, Jaycox JR. Diverse functional autoantibodies in patients with COVID-19. *Nature* 2021; 595:283-288.
33. Nunez-Castilla J, Stebliankin V, Baral P, Balbin CA, Sobhan M, Cickovski T et al. Potential autoimmunity resulting from molecular mimicry between SARS-CoV-2 spike and human proteins. *Viruses* 2022; 14:1415.
34. Cabral-Marques O, Halpert G, Schimke LF, Ostrinski Y, Vojdani A, Lattin MT. Autoantibodies targeting GPCRs and RAS-related molecules associated with COVID-19 severity. *Nature Communications* 2022; 13:1220.
35. Arthur JM, Forrest JC, Boehme KW, Kennedy JL, Owens S, Liu J. Development of ACE2 autoantibodies after SARS-CoV-2 infection. *PloS ONE* 2021; 16:e0257016.
36. Wallukat G, Hohberger B, Wenzel K, Furst J, Wallukat A. Functional autoantibodies against G-protein coupled receptors in patients with persistent Long-Covid-19 symptoms. *Journal of Translational Autoimmunity* 2021; 4:100100.
37. Levine TD, Kafaie J, Zeidman LA, Saperstein DS, Bland RJ. Cryptogenic small-fiber neuropathies: Serum autoantibody binding to trisulfated heparin disaccharide and fibroblast growth factor receptor-3. *Muscle & Nerve* 2020; 61:512-515.
38. Oaklander AL, Mills AJ, Kelley M, Toran MK. Peripheral neuropathy evaluations of patients with prolonged long COVID. *Neurol Neuroimmunol Neuroinflamm* 2022; 9:e1146.
39. Burakgazi AZ. Small-fiber neuropathy possibly associated with COVID-19. *Case Rep Neurol* 2022; 14:208-212.
40. Shouman K, Vanichkachorn G, Chesire WP, Suarez MD, Shelly S. Autonomic dysfunction following COVID-19 infection: an early experience. *Clinical Autonomic Research* 2021; 31:385-394.

41. Hinduja A, Moutairou A, Calvet JH. Sudomotor dysfunction in patients recovered from COVID-19. *Clinical Neurophysiology* 2021; 51:193-196.
42. Abdelnour L, Abdalla ME, Babiker S. COVID 19 infection presenting as motor peripheral neuropathy. *Journal of the Formosan Medical Association* 2020; 119:1119-1120.
43. Abrams RM, Simpson DM, Navis A, Jette N, Zhou L. Small fiber neuropathy associated with SARS-CoV-2 infection. *Muscle & Nerve* 2021.
44. Zhou L, Shin S. Small fiber neuropathy. *Practical Neurology* 2021;36.
45. Bednarik J, Bursova S, Dusek L, Sommer C. Etiology of small-fiber neuropathy. *Journal of the Peripheral Nervous System* 2009; 14:177-183.
46. Theoharides TC, Tsilioni I, Ren H. Recent advances in our understanding of mast cell activation- or should it be mast cell mediator disorders? *Expert Rev Clin Immunol* 2019; 15:639-656.
47. Weinstock LB, Brook JB, Walters AS, Goris A, Afrin LB, Molderings GJ. Mast cell activation symptoms are prevalent in Long-COVID. *International Journal of Infectious Diseases* 2021; 112:217-226.
48. Gold JE, Okyay R, Licht WE, Hurley DJ. Investigation of Long COVID prevalence and its relationship to Epstein-Barr Virus reactivation. *Pathogens* 2021; 10:763.
49. Chen T, Song J, Liu H, Zheng H, Chen C. Positive Epstein-Barr virus detection in coronavirus disease 2019 (COVID-19) patients. *Scientific Reports* 2021; 11:10902.
50. Le Balc'h P, Pinceaux K, Pronier C, Seguin P, Reizine F. Herpes simplex virus and cytomegalovirus reactivations among severe COVID-19 patients. *Crit Care* 2020; 24:530.
51. Peluso MJ, Deveau TM, Munter SE, Ryder D, Buck A, Lu S et al. Evidence of recent Epstein-Barr virus reactivation in individuals experiencing Long Covid. *medRxiv* 2022.
52. Pont G, Pastorino L, Manfredini M, Ozben T, Oliva G, Kaleci S. COVID-19 spreading across world correlates with C677T allele of the methylenetetrahydrofolate reductase (MTHFR) gene prevalence. *J Clin Lab Anal* 2021; 35:e23798.
53. Karst M, Hollenhorst J, Achenbach J. Life-threatening course in coronavirus disease 2019 (COVID-19): Is there a link to methylenetetrahydrofolic acid reductase (MTHFR) polymorphism and hyperhomocysteinemia? *Medical Hypotheses* 2020; 114:110234.
54. Carpene G, Negrini D, Henry BM, Montagnana L, Lippi G. Homocysteine in coronavirus disease (COVID-19): a systematic literature review. *Diagnosis* 2022.
55. Ponti G, Roli L, Oliva G, Manfredini M, Trenti T, Kaleci S et al. Homocysteine (Hcy) assessment to predict outcomes of hospitalized COVID-19 patients: a multicenter study on 313 Covid-19 patients. *Clin Chem Lab Med* 2021; 59:e354-e357.

56. Abu-Farha M, Al-Sabah S, Hammad MM, Hebbar P, John SE, Taher I et al. Prognostic genetic markers for thrombosis in COVID-19 patients: A focused analysis on D-Dimer, homocysteine and thromboembolism. *Frontiers in Pharmacology* 2020; 11:587451.
57. Duma D, Collins JB, Chou JW, Cidlowski JA. Sexually dimorphic actions of glucocorticoids provide a link to inflammatory diseases with gender differences in prevalence. *Science Signaling* 2010; 3(143):ra74.
58. Atoui A, Jarrah K, Al Mahmassani L, Bou-Fakhredin R, Taher AT. Deep venous thrombosis and pulmonary embolism after COVID-19 mRNA vaccination. *Ann Hematol* 2022; 101:1111-1113.
59. Tomassetti F, Nuccetelli M, Sarubbi S, Gisone F, Ciotti M. Evaluation of S-RBD and high specificity ACE-2 binding antibodies on SARS-CoV-2 patients after six months from infection. *International Immunopharmacology* 2021; 99:108013.
60. Fung J, Moore J. *The complete guide to fasting*. Victory Belt Publishing; 2016.
61. deCabo R, Mattson MP. Effects of intermittent fasting on health, aging, and disease. *N Engl J Med* 2019; 381:2541-2551.
62. Hannan A, Rahman A, Rahman S, Sohag AA, Dash R, Uddin J. Intermittent fasting, a possible priming tool for host defense against SARS-CoV-2 infection: Crosstalk among calorie restriction, autophagy and immune response. *Immunology Letters* 2020; 226:38-45.
63. Zhao Y, Jia M, Chen W, Liu Z. The neuroprotective effects of intermittent fasting on brain aging and neurodegenerative diseases via regulating mitochondrial function. *Free Radical Biology & Medicine* 2022; 182:206-218.
64. Beckman JA. Thrombolytic therapy for pulmonary embolism. *JAMA* 2014; 311:2385-2386.
65. Cheng CW, Adams GB, Perin L, Wei M, Zhou X, Lam BS. Prolonged fasting reduces IGF-1/PKA to promote hematopoietic-stem-cell-based regeneration and reverse immunosuppression. *Cell Stem Cell* 2014; 14:810-823.
66. Hine C, Mitchell JR. Saying No to drugs: Fasting protects hematopoietic stem cells from chemotherapy and aging. *Cell Stem Cell* 2014; 14:704.
67. Mostafa DK, Khedr MM, Barakat MK, Abdellatif AA, Elsharkawy AM. Autophagy blockade mechanistically links proton pump inhibitors to worsened diabetic nephropathy and aborts the renoprotection of metformin/enalapril. *Life Sci* 2021; 265:118818.
68. Xu R, Ji Z, Xu C, Zhu J. The clinical value of using chloroquine or hydroxychloroquine as autophagy inhibitors in the treatment of cancers. A systematic review and meta-analysis. *Medicine* 2018; 97:46.
69. Sotelo J, Briceno E, Lopez-Gonzalez MA. Adding chloroquine to conventional treatment for glioblastoma multiforme: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 2006; 144:337-343.

70. Wolpin BM, Rubinson DA, Wang X, Chan JA, Cleary JM, Enzinger PC et al. Phase II and pharmacodynamic study of autophagy inhibition using hydroxychloroquine in patients with metastatic pancreatic adenocarcinoma. *The Oncologist* 2014; 19:637-638.
71. Amaravadi RK, Kimmelman AC, Debnath J. Targeting autophagy in cancer: Recent advances and future directions. *Cancer Discov* 2019; 9:1167-1181.
72. Zeh HJ, Bahary N, Boone BA, Singh AD, Normolle Dp, Hogg ME. A randomized Phase II preoperative study of autophagy inhibition with high-dose hydroxychloroquine and Gemcitabine/Nab-Paclitaxel in pancreatic cancer patients. *Clinical Cancer Research* 2020; 26:3126-3134.
73. Minois N, Bauer MA, Rockenfeller P, Eisneber T, Brandhorst S, Kroemer G. Spermidine promotes stress resistance in *Drosophila melanogaster* through autophagy-dependent and -independent pathways. *Cell Death and Disease* 2012; 3:e401.
74. Gassen NC, Papiés J, Bajaj T, Emanuel J, Wechmann K, Heinz DE et al. Analysis of SARS-CoV-2 controlled autophagy reveals spermidine, MK-2206, and niclosamide as putative antiviral therapeutics. *bioRxiv* 2020.
75. Eisenberg T, Abdellatif M, Schroeder S, Primessnig U, Stekovic S, Pendl T et al. Cardioprotection and lifespan extension by natural polyamine spermidine. *Nat Med* 2016; 22:1428-1438.
76. Kiechl S, Pechlaner R, Willeit P, Notdurfier M, Paulweber B, Willeit K et al. Higher spermidine intake is linked to lower mortality: a prospective population-based study. *Am J Clin Nutr* 2018; 108:371-380.
77. Madeo F, Carmona-Gutierrez D, Kepp O, Kroemer G. Spermidine delays aging in humans. *Aging* 2022; 10:2209-2211.
78. Minois N, Carmona-Gutierrez D, Madeo F. Polyamines in aging and disease. *Aging* 2011; 3:1-17.
79. Ci X, Li H, Yu Q, Zhang X, Yu L, Chen N et al. Ivermectin exerts anti-inflammatory effect by downregulating the nuclear transcription factor kappa-B and mitogen activated protein kinase pathway. *Fundamental & Clinical Pharmacology* 2009; 23:449-455.
80. DiNicolantonio JJ, Barroso-Arranda J, McCarty M. Ivermectin may be a clinically useful anti-inflammatory agent for late-stage COVID-19. *Open Heart* 2020; 7:e001350.
81. Yan S, Ci X, Chen N, Chen C, Li X, Chu X et al. Anti-inflammatory effects of ivermectin in mouse model of allergic asthma. *Inflamm Res* 2011; 60:589-596.
82. Saha JK, Raihan J. The binding mechanism of ivermectin and levosalbutamol with spike protein of SARS-CoV-2. *Research Square* 2021.
83. Bello M. Elucidation of the inhibitory activity of ivermectin with host nuclear importin alpha and several SARS-CoV-2 targets. *Journal of Biomolecular Structure and Dynamics* 2021.

84. Lehrer S, Rheinstein PH. Ivermectin docks to the SARS-CoV-2 spike receptor-binding domain attached to ACE2. *In Vivo* 2020; 34:3023-3026.
85. Nicolas P, Maia MF, Bassat Q, Kobylinski KC, Monteiro W. Safety of oral ivermectin during pregnancy: a systematic review and meta-analysis. *Lancet Glob Health* 2020; 8:e92-e100.
86. Younger J, Parkitny L, McLain D. The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain. *Clin Rheumatol* 2014; 33:451-459.
87. Toljan K, Vrooman B. Low-dose naltrexone (LDN) - Review of therapeutic utilization. *Med Sci* 2018; 6:82.
88. Molina-Carballo A, Palacios-Lopez R, Jerez-Calero A, Agil A. Protective effect of melatonin administration against SARS-CoV-2 infection: A systematic review. *Current Issues in Molecular Biology* 2022; 44:31-45.
89. Hasan ZT, AlAtrakji MQ, Mehuaiden AK. The effect of melatonin on thrombosis, sepsis and mortality rate in COVID-19 patients. *International Journal of Infectious Diseases* 2022; 114:79-84.
90. Reiter RJ, Sharma R, Ma Q, Liu C, Manucha W, Abreu-Gonzalez P. Plasticity of glucose metabolism in activated immune cells: advantages for melatonin inhibition of COVID-19 disease. *Melatonin Res* 2020; 3:362-379.
91. Reiter RR, Sharma R, Castillo R, Marik PE, Rodriguez AD, Cardinali DP. Coronavirus-19, Monocyte/Macrophage glycolysis and inhibition by melatonin. *J SARS-CoV2 COVID* 2021; 2:29-31.
92. Colunga Biancatelli RM, Berrill M, Mohammed YH, Marik PE. Melatonin for the treatment of sepsis: the scientific rationale. *J Thorac Dis* 2020; 12 (Suppl 1):S54-S65.
93. Marik PE. Hydrocortisone, Ascorbic Acid and Thiamine (HAT therapy) for the treatment of sepsis. Focus on ascorbic acid. *Nutrients* 2018; 10:1762.
94. Marik PE. Vitamin C for the treatment of sepsis: The scientific rationale. *Pharmacol Therapeut* 2018; 189:63-70.
95. Colunga Biancatelli RM, Berrill M, Marik PE. The antiviral properties of vitamin C. *Expert Rev Anti Infect Ther* 2020; 18:99-101.
96. Miranda-Massari JR, Toro AP, Loh D, Rodriguez JR, Borges RM. The effects of vitamin C on the multiple pathological stages of COVID-19. *Life* 2021; 11:1341.
97. Holford P, Carr AC, Zawari M, Vizcaychipi MP. Vitamin C intervention for Critical COVID-19: A pragmatic review of the current level of evidence. *Life* 2021; 11:1166.
98. Islam MT, Guha B, Hosen S, Alam T, Shahadat S. Nigellalogy: A review on Nigella Sativa. *MOJ Bioequiv Availab* 2017; 3:00056.

99. Barbash IJ, Davis BS, Yabes JG, Seymour CW, Angus DC, Kahn JM. Treatment patterns and clinical outcomes after the introduction of the Medicare Sepsis Performance Measure (SEP-1). *Ann Intern Med* 2021.
100. Ashraf S, Ashraf S, Ashraf M, Imran MA, Kalsoom L, Siddiqui UN et al. Honey and *Nigella sativa* against COVID-19 in Pakistan (HNS-COVID-PK): A multi-center placebo-controlled randomized clinical trial. *medRxiv* 2021.
101. Fakhar-e-Alam Kulyar M, Li R, Mehmood K, Waqas M, Li K, Li J. Potential influence of *Nigella sativa* (Black cumin) in reinforcing immune system: A hope to decelerate the COVID-19 pandemic. *Phytomedicine* 2021; 85:153277.
102. Hannan MA. Black Cumin (*Nigella sativa* L.): A Comprehensive Review on Phytochemistry, Health Benefits, Molecular Pharmacology, and Safety. *Nutrients* 2021; 13(6).
103. Warner ME, Naranjo J, Pollard EM, Weingarten TN, Warner MA. Serotonergic medications, herbal supplements, and perioperative serotonin syndrome. *Can J Anaesth* 2017; 64:940-946.
104. Gutierrez-Castrellon P, Gandara-Marti T, Abreu AT, Nieto-Rufino CD, Lopez-Orduna E. Probiotic improves symptomatic and viral clearance in Covid-19 outpatients: a randomized, quadruple-blinded, placebo-controlled trial. *GUT Microbes* 2022; 14:e2018899.
105. Zuo T, Wu X, Wen W, Lan P. Gut microbiome alterations in COVID-19. *Genomics, Proteomics & Bioinformatics* 2021.
106. Chen Y, Gu S, Chen Y, Lu H, Shi D, Guo J. Six-month follow-up of gut microbiota richness in patients with COVID-19. *Gut* 2021.
107. Rosa DD, Dias MM, Grzeskowiak LM, Reis SA. Milk kefir: nutritional, microbiological and health benefits. *Nutrition Research Reviews* 2017; 30:82-96.
108. Thomas R, Aldous J, Forsyth R, Chater A, Williams M. The influence of a blend of probiotic *Lactobacillus* and prebiotic inulin on the duration and severity of symptoms among individuals with COVID-19. *Infect Dis Diag Treat* 2022; 5:12.
109. Lee CR, Zeldin DC. Resolvin infectious inflammation by targeting the host response. *N Engl J Med* 2015; 373:2183-2185.
110. Serhan CN. Novel pro-resolving lipid mediators in inflammation are leads for resolution physiology. *Nature* 2014; 510:92-101.
111. Servy EJ, Jacquesson-Fournols L, Cohen M, Menezo YJ. MTHFR isoforms carriers. 5-MTHF (5-methyl tetrahydrofolate) vs folic acid: a key to pregnancy outcome: a case series. *Journal of Assisted Reproduction and Genetics* 2018; 35:1431-1435.
112. Shukla AM, Shukla AW. Expanding horizons for clinical applications of chloroquine, hydroxychloroquine and related structural analogues. *Drugs in Context* 2019; 8:2019-9-1.

113. Plantone D, Koudriavtseva T. Current and future use of chloroquine and hydroxychloroquine in infectious, immune, neoplastic and neurological diseases: A mini review. *Clin Drug Invest* 2018; 38:653-671.
114. Ruiz-Irastorza G, Khamashta MA. Hydroxychloroquine: the cornerstone of lupus therapy. *Lupus* 2008; 17:271-273.
115. de Moreuil C, Alavi Z, Pasquier E. Hydroxychloroquine may be beneficial in preeclampsia and recurrent miscarriage. *Br J Clin Pharmacol* 2020; 86:39-49.
116. Siso A, Ramos-Casals M, Bove A, Soria N, Testi A, Plaza J. Previous antimalarial therapy in patients diagnosed with lupus nephritis: Influence on outcomes and survival. *Lupus* 2008; 17:281-288.
117. Misra HS, rajpurohit YS, Khairnar NP. Pyrroloquinoline-quinone and its versatile roles in biological processes. *J Biosci* 2012; 37:312-325.
118. Akagawa M, Nakano M, Ikemoto K. Recent progress in studies on the health benefits of pyrroloquinoline quinone. *Bioscience, Biotechnology, and Biochemistry* 2016; 80:13-22.
119. Hamilton D, Jensen GS. Nutraceutical support of mitochondrial function associated with reduction of long-term fatigue and inflammation. *Alternative Therapies in Health & Medicine* 2021; 27:8-18.
120. Nicolson GL, Settineri R, Ellithorpe R. Lipid replacement therapy with a glycolipid formulation of NADH and CoQ10 significantly reduces fatigue in intractable chronic fatiguing illnesses and chronic lyme disease patients. *International Journal of Clinical Medicine* 2012; 3:163-170.
121. Chowanadisai W, Bauerly KA, Tchapanian E, Wong A, Rucker RB. Pyrroloquinoline quinone stimulates mitochondrial biogenesis through cAMP response element-binding protein phosphorylation and increased PGC-1 α expression. *J Biol Chem* 2010; 285:142-152.
122. Nicolson GL, Settineri R. Lipid replacement therapy: a functional food approach with new formulations for reducing cellular oxidative damage, cancer-associated fatigue and the adverse effects of cancer therapy. *Functional Foods in Health and Disease* 2011; 1:135-160.
123. Nicolson GL, Rosenblatt S, de Mattos GF, Settineri R, Breeding PC, Ash ME. Clinical uses of membrane lipid replacement supplements in restoring membrane function and reducing fatigue in chronic disease and cancer. *Discoveries* 2016; 4:e54.
124. Izquierdo JL, Soriano JB, Gonzalez Y, Lumbreras S. Use of N-Acetylcysteine at high doses as an oral treatment for patients with COVID-19. *Science Progress* 2022; 105.
125. Shi Z, Puyo CA. N-Acetylcysteine to combat COVID-19: an evidence review. *Therapeutics and Clinical Risk Management* 2020; 16:1047-1055.
126. De Flora S, Balansky R, La Maestra S. Rationale for the use of N-acetylcysteine in both prevention and adjuvant therapy of COVID-19. *FASEB J* 2020.

127. Schmitt B, Vicenzi M, Garrel C, Denis FM. Effects of N-acetylcysteine, oral glutathione (GSH) and a novel sublingual form of GSH on oxidative stress markers: A comparative crossover study. *Redox Biology* 2015; 6:198-205.
128. Allen J, Bradley RD. Effects of oral glutathione supplementation on systemic oxidative stress biomarkers in human volunteers. *Journal of Alternative & Complementary Medicine* 2011; 17:827-833.
129. Saeedi-Boroujeni A, Mahmoudian-Sani MR. Anti-inflammatory potential of Quercetin in COVID-19 treatment. *J Inflamm* 2021; 18:3.
130. Valentova K, Vrba J, Bancirova M, Ulrichova J. Isoquercitrin: Pharmacology, toxicology, and metabolism. *Food and Chemical Toxicology* 2014; 68:267-282.
131. Leyva-Lopez N, Gutierrez-Grijalva EP, Ambriz-Perez D. Flavonoids as cytokine modulators: A possible therapy for inflammation-related diseases. *Int J Mol Sci* 2016; 17:921.
132. Karimi A, Naeini F, Azar VA, Hasanzadeh M. A comprehensive systematic review of the therapeutic effects and mechanisms of action of quercetin in sepsis. *Phytomedicine* 2021; 86:153567.
133. Jo S, Kim S, Shin DH, Kim MS. Inhibitions of SARS-CoV 3CL protease by flavonoids. *Journal of Enzyme Inhibition and Medicinal Chemistry* 2020; 35:145-151.
134. Li Y, Yao J, Han C, Yang J, Chaudhry MT, Wang S et al. Quercetin, inflammation and immunity. *Nutrients* 2016; 8:8030167.
135. Nair MP, Kandaswami C, Mahajan S, Chadha KC, Chawda R, Nair H. The flavonoid, quercetin, differentially regulates Th-1 (INF) and Th-2 (IL4) cytokine gene expression by normal peripheral blood mononuclear cells. *Biochimica et Biophysica Acta* 2020; 1593:29-36.
136. Derosa G, Maffioli P, D'Angelo A, Di Pierro F. A role for quercetin in coronavirus disease 2019 (COVID-19). *Phytotherapy Research* 2020.
137. Weng Z, Zhang B, Asadi S, Sismanopoulos N, Butcher A. Quercetin is more effective than cromolyn in blocking human mast cell cytokine release and inhibits contact dermatitis and photosensitivity in humans. *PLoS ONE* 2012; 7:e33805.
138. Calis Z, Mogulkoc R, Baltaci AK. The roles of flavonols/flavonoids in neurodegeneration and neuroinflammation. *Mini Rev Med Chem* 2020; 20:1475-1488.
139. Rich GT. Towards an Understanding of the Low Bioavailability of Quercetin: A Study of Its Interaction with Intestinal Lipids. *Nutrients* 2017; 9(2).
140. Riva A, Ronchi M, Petrangolini G, Bosisio S, Allegrini P. Improved oral absorption of quercetin from quercetin phytosome, a new delivery system based on food grade lecithin. *European Journal of Drug Metabolism and Pharmacokinetics* 2019; 44:169-177.

141. Wang W, Sun C, Mao L, Ma P, Liu F, Yang J. The biological activities, chemical stability, metabolism and delivery systems of quercetin: A review. *Trends in Food Science & Technology* 2016; 56:21-38.
142. Rondanelli M, Perna S, Gasparri C, Petrangolini G, Cavioni A, Peroni G. Promising effects of a 3-month period of quercetin phytosome supplementation in the prevention of symptomatic COVID-19 disease in healthcare workers: A pilot study. *Life* 2022; 12:66.
143. DiPierro F, Derosa G, Maffioli P, Togni S, Riva A. Possible therapeutic effects of adjuvant Quercetin supplementation against early stage COVID-19 infection: A prospective, randomized, controlled, and open-label study. *International journal of general medicine* 2021; 14:2359-2366.
144. Sathyapalan T, Manuchehri AM, Thatcher NJ, Rigby AS, Chapman T. The effect of soy phytoestrogen supplementation on thyroid status and cardiovascular risk markers in patients with subclinical hypothyroidism: A randomized, double-blind, crossover study. *J Clin Endocrinol Metab* 2020; 96:1422-1449.
145. Sanabria-Mazo JP, Montero-Marin J, Feliu-Soler A, Gasion V, Navarro-Gil M. Mindfulness-based program plus amygdala and insula retraining (MAIR) for the treatment of women with fibromyalgia: A pilot randomized controlled trial. *J Clin Med* 2020; 9:3246.
146. Yong SJ. Long-haul COVID-19: Putative pathophysiology, risk factors, and treatments. *medRxiv* 2020.
147. Shu C, Feng S, Cui Q, Cheng S, Wang Y. Impact of Tai Chi on CRP, TNF-alpha and IL-6 in inflammation: a systematic review and meta-analysis. *Ann Palliat Med* 2021; 10:7468-6478.
148. Zhang Z, Ren JG, Guo JL, An L, Li S, Zhang ZC. Effects of Tai Chi and Qigong on rehabilitation after COVID-19: a protocol for systematic review and meta-analysis. *BMJ Open* 2022; 12:e059067.
149. Falkenberg RI, Eising C, Peters ML. Yoga and immune system functioning: a systematic review of randomized controlled trials. *J Behav Med* 2018; 41:467-482.
150. Brown JT, Saigal A, Karia N, Patel RK, Razvi Y, Steeden JA. Ongoing exercise intolerance following COVID-19: A magnetic resonance-Augmented Cardiopulmonary exercise Test Study. *J Am Heart Assoc* 2022; 11:e024207.
151. Robbins T, Gonevski M, Clark C, Sharma K, Magar A. Hyperbaric oxygen therapy for the treatment of long COVID: early evaluation of a highly promising intervention. *Clinical Medicine* 2021; 21:e629-e632.
152. Oliaei S, Mehrtak M, Karimi A, Noori T, Shojaei A, Dadras O. The effects of hyperbaric oxygen therapy (HBOT) on coronavirus disease-2019 (COVID-19): a systematic review. *Eur J Med Res* 2021; 26:96.
153. Senniappan K, Jeyabalan S, Rangappa P, Kanchi M. Hyperbaric oxygen therapy: Can it be a novel supportive therapy in COVID-19? *Indian Journal of Anaesthesia* 2020; 64:835-841.

154. Kjellberg A, De Maio A, Lindholm P. Can hyperbaric oxygen safely serve as an anti-inflammatory treatment for COVID-19? *Medical Hypotheses* 2020; 144:110224.
155. Hadanny A, Abbott S, Suzin G, Bechor Y, Efrati S. Effect of hyperbaric oxygen therapy on chronic neurocognitive deficits of post-traumatic brain injury patients: retrospective analysis. *BMJ Open* 2018; 8:e023387.
156. Han CH, Zhang PX, Xu WG, Li RP. Polarization of macrophages in the blood after decompression in mice. *J Appl Physiol* 2017; 117(2):240.
157. De Maio A, Hightower LE. COVID-19, acute respiratory distress syndrome (ARDS), and hyperbaric oxygen therapy (HBOT): what is the link? *Cell Stress & Chaperones* 2020; 25:717-720.
158. Buras JA, Holt D, Orlow D, Belikoff B, Pavildes S, Reenstra WR. Hyperbaric oxygen protects from sepsis mortality via an interleukin-10-dependent mechanism. *Crit Care Med* 2006; 34:2624-2629.
159. Tezgin D, Giardina C, Perdrizet GA, Hightower LE. The effect of hyperbaric oxygen on mitochondrial and glycolytic energy metabolism: the caloristasis concept. *Cell Stress and Chaperones* 2020; 25:667-677.
160. Mogil RJ, Kaste SC, Ferry RJ, Hudson MM, Howell CR. Effect of low-magnitude, high-frequency mechanical stimulation on BMD among young childhood cancer survivors. A randomized clinical trial. *JAMA Oncol* 2016; 2:908-915.
161. Jamme M, Mazeraud A. Plasmapheresis efficiency in Coronavirus disease 2019: More related to what you add and not what you take away? *Crit Care Med* 2021.
162. Patidar GK, Land KJ, Vrieling H, Dann EJ, Spitalnik SL. Understanding the role of therapeutic plasma exchange in COVID-19: preliminary guidance and practices. *Vox Sanguinis* 2021.
163. Hashemian SM, Shafiq N, Afzal G, Jamaati H, Tabarsi P, Marjani M. Plasmapheresis reduces cytokine and immune cell levels in COVID-19 patients with acute respiratory distress syndrome (ARDS). *Pulmonary* 2021; 27:486-492.
164. Balaghali S, Dabbaghi R, Eshghi P, Mousavi SA, Heshmati F, Mohammadi S. Potential of therapeutic plasmapheresis in treatment of COVID-19 patients: immunopathogenesis and coagulopathy. *Transfusion and Apheresis Science* 2020; 59:102993.
165. Keith P, Day M, Perkins L, Moyer L, Hewitt K, Wells A. A novel treatment approach to the novel coronavirus: an argument for the use of therapeutic plasma exchange for fulminant COVID-19. *Crit Care* 2020; 24:128.
166. Morath C, Weigand MA, Zeier M, Speer C, Tiwari-Heckler S. Plasma exchange in critically ill COVID-19 patients. *Crit Care* 2020; 24:481.
167. Fernandez J, Gratacos-Gines J, Olivas P, Costa M, Nieto S, Mateo D. Plasma exchange: An effective rescue therapy in critically ill patients with Coronavirus Disease 2019 infection. *Crit Care Med* 2020.

168. Gucyetmez B, Atalan HK, Sertdemir I, Cakir U, Telci L. Therapeutic plasma exchange in patients with COVID-19 pneumonia in intensive care unit: a retrospective study. *Crit Care* 2020; 24:492.
169. Kiprof DD, Herskowitz A, Kim D, Lieb M, Liu C, Watanabe E. Case report. Therapeutic and immunomodulatory effects of plasmapheresis in long-haul COVID. *F1000Research* 2022; 10:1189.
170. Mostafa-Hedeab G, Al-kuraishy HM, Al-Gareeb AA, Jeandet P, Saaad HM, El-Saber Batiha G. A raising dawn of pentoxifylline in the management of inflammatory disorders in Covid-19. *Inflammopharmacology* 2022.
171. Patterson B, Yogendra R, Guevara-Coto J, Osgood E, Bream J, Parikh P. Targeting the monocytic-endothelial-platelet axis with maraviroc and pravastatin as a therapeutic option to treat long COVID/Post-acute sequelae of COVID (PASC). *Research Square* 2022.
172. Pitt B, Sutton NR, Wang Z, Holinstat M. Potential repurposing of the HDAC inhibitor valproic acid for patients with COVID-19. *Eur J Pharmacol* 2021; 898:173988.
173. Unal G, Turan B, Balcioglu YH. Immunopharmacological management of COVID-19: Potential therapeutic role of valproic acid. *Medical Hypotheses* 2020; 14:109891.
174. Wu C, Li A, Leng Y, Kang J. Histone deacetylase inhibition by sodium valproate regulates polarization of macrophage subsets. *DNA and Cell Biology* 2012; 31:592-599.
175. Larsson P, Alwis I, Niego B, Glise L, Daglas M, Jackson SP. Valproic acid selectively increases vascular endothelial tissue -type plasminogen activator production and reduces thrombus formation in the mouse. *J Thromb Haemost* 2016; 14:2496-2508.
176. Santamarina MG, Boisier D, Contreras R, Baque M, Volpacchio M. COVID-19: a hypothesis regarding the ventilation-perfusion mismatch. *Crit Care* 2020; 24:395.
177. Mario L, Roberto M, Marta L, Teresa CM, Laura M. Hypothesis of COVID-19 therapy with sildenafil. *International Journal of Preventive Medicine* 2020; 11:76.
178. Santamarina MG, Beddings I, Martinez Lomakin F, Boisier Riscal D. Sildenafil for treating patients with COVID-19 and perfusion mismatch: a pilot randomized trial. *Crit Care* 2022; 26:1.
179. Kniotek M, Boguska A. Sildenafil can affect innate and adaptive immune system in both experimental animals and patients. *Journal of Immunology Research* 2017; 2017:4541958.
180. Isidori AM, Giannetta E, Pofi R, Venneri MA, Gianfrilli D, Campolo F. Targeting the NO-cGMP-PDE5 pathway in COVID-19 infection. The DEDALO project. *Andrology* 2021; 9:33-38.
181. Al-kuraishy HM, Ali-Gareeb AI, Al-Niemi MS, Buhadily AK. COVID-19 and phosphodiesterase enzyme type 5 inhibitors. *J Microsc Ultrastruct* 2022; 8:141-145.
182. Houghton CA, Fassett RG, Coombes JS. Sulforane: translational research from laboratory bench to clinic. *Nutr Rev* 2013; 71:709-726.

183. Kim JK, Park SU. Current potential health benefits of sulforaphane. *EXCLI Journal* 2016; 15:571-577.
 184. Mokhtari RB, Baluch N, Homayouni TS, Kumar S, Yeger H. The role of sulforaphane in cancer chemoprevention and health benefits: a mini-review. *J Cell Commun Signal* 2018; 12:91-101.
 185. Clarke JD, Hsu A, Riedl K, Bella D, Stevens JF, Ho E. Bioavailability and inter-conversion of sulforaphane and erucin in human subjects consuming broccoli sprouts or broccoli supplement in a cross-over study design. *Pharmacol Res* 2011; 64:456-463.
 186. Khandouzi N, Shidfar F, Rajab A, Rahideh T, Hosseini P, Taheri MM. The effects of Ginger on fasting blood sugar, hemoglobin A1C, Apolipoprotein B, Apolipoprotein A-1 and malondialdehyde in type 2 diabetic patients. *Iranian Journal of Pharmaceutical Research* 2015; 14:131-140.
 187. Gonzalez-Castejon M, Visioli F, Rodrigues-Casado A. Diverse biological activities of dandelion. *Nutr Rev* 2012; 70:534-547.
 188. Olas B. New perspectives on the effect of dandelion, its food products and other preparations on the cardiovascular system and its diseases. *Nutrients* 2022; 14:1350.
 189. Tran HT, Gigl M, Le NP, Dawid C, Lamy E. In Vitro effect of *Taraxacum officinale* leaf aqueous extract on the interaction between ACE2 cell surface receptor and SARS-CoV-2 spike protein D614 and four mutants. *Pharmaceuticals* 2021; 14:1055.
 190. "Taraxaci folium" and "taraxaci radix". Monography on the Medicinal Uses of Plant Drugs. End.ed., 499-504. 2003. Stuttgart, Germany, Thieme.
- Ref Type: Serial (Book,Monograph)
191. Harasstaini OA, Moin S, Tham CL, Liew CY, Ismail N, Israif DA. Flavonoid combinations cause synergistic inhibition of proinflammatory mediator secretion form lipopolysaccharide-induced RAW 264.7 cells. *Inflammation Research* 2010; 59:711-721.
 192. Marforio TD, Mattioli EJ, Zerbetto F, Calvaresi M. Fullerenes against COVID-19: Repurposing C50 and C70 to clog the active site of SARS-CoV-2 protease. *Molecules* 2022; 27:1916.
 193. Hurmach Vv, Platonov MO, Prylutska SV, Scharff P, Ritter U. C60 fullerene against SARS-CoV-2 coronavirus: an in silico insight. *Scientific Reports* 2021; 11:17748.
 194. Shevchuk N. Adapted cold shower as a potential treatment for depression. *Medical Hypotheses* 2008; 70:995-1001.
 195. Mooventhan A, Nivethitha L. Scientific evidence-based effects of hydrotherapy on various systems of the body. *North American Journal of Medical Sciences* 2014; 6:199-209.
 196. Hong J, Barnes MJ, Kessler NJ. Case study: Use of vibration therapy in the treatment of diabetic peripheral small fiber neuropathy. *International Journal of Diabetes Mellitus* 2015; 3:72-75.

197. Kessler NJ, Hong J. Whole body vibration therapy for painful diabetic peripheral neuropathy: A Pilot study. *Journal of Bodywork & Movement Therapies* 2013; 17:518-522.
198. Sanna A, Firinu D, Zavattari P, Valera P. Zinc status and autoimmunity: A systematic review and meta-analysis. *Nutrients* 2018; 10:68.
199. Diep PT, Buemann B, Uvnas-Moberg K. Oxytocin, a possible treatment for COVID-19? everything to gain, nothing to lose. *Clinical Neuropsychiatry* 2020; 17:192-195.
200. Leuner B, Caponiti JM, Gould E. Oxytocin stimulates adult neurogenesis even under conditions of stress and elevated glucocorticoids. *Hippocampus* 2012; 22:861-868.
201. MacDonald K, McDonald TM. The peptide that binds: A systematic review of oxytocin and its prosocial effects in humans. *Harv Rev Psychiatry* 2010; 18:1-21.
202. Matsushita H, Latt HM, Koga Y, Nishiki T, Matsui H. Oxytocin and stress: Neural mechanisms, stress-related disorders, and therapeutic approaches. *Neuroscience* 2019; 417:1-10.
203. Tzabazis A, Kori S, Mechanic J, Miller J, Pascual C, Carson D. Oxytocin and migraine headache. *Headache* 2017; 57:64-75.
204. Krause DN, Warfvinge K, Haanes KA, Edvinsson L. Hormonal influences in migraine - interactions of oestrogen, oxytocin and CGRP. *Nature Reviews Neurology* 2021; 17:621-633.
205. Freitag K, Sterczyk N, Wendlinger S, Schulz J, Ralser M, Fleck L et al. Spermidine reduces neuroinflammation and soluble amyloid beta in an Alzheimer's disease mouse model. *Journal of Neuroinflammation* 2022; 19:172.
206. Schroeder S, Hofer S, Zimmermann A, Pechlaner R, Pendl T, Bergmann M et al. Dietary spermidine improves cognitive function. *Cell Reports* 2021; 35:108985.
207. Blaylock RL. Vaccines, depression, and neurodegeneration after age 50 years: another reason to avoid the recommended vaccines. *Medical Veritas* 2008; 5:1742-1747.
208. Pappa S, Barmparessou Z, Sakka E, Sakkas N, Pappas A. Depression, Insomnia and post-traumatic stress disorder in COVID-19 survivors: Role of gender and impact on quality of life. *J Pers Med* 2022; 12:486.
209. Porter C, Favara M, Scott D, Craske MG, Stein A. Impact of the COVID-19 pandemic on anxiety and depression symptoms of young people in the Global South: evidence from a four-country cohort study. *medRxiv* 2021.
210. Lau T, Horschitz S, Berger S, Bartsch D, Schloss P. Antidepressant-induced internalization of the serotonin transporter in serotonergic neurons. *FASEB J* 2008; 22:1702-1714.
211. Renoir T. Selective serotonin reuptake inhibitor antidepressant treatment discontinuation syndrome: a review of the clinical evidence and the possible mechanisms involved. *4* 2013;(45).

212. Hengartner MP, Ploderi M. Newer-generation antidepressants and suicide risk in randomized controlled trials: A re-analysis of the FDA database. *Psychother Psychosom* 2019; 88:247-248.
213. Hengartner MP, Amendola S, Kaminski JA. Suicide risk with selective serotonin reuptake inhibitors and other new-generation antidepressants in adults: a systematic review and meta-analysis of observational studies. *J Epidemiol Community Health* 2021; 75:523-530.
214. Antidepressants and Violence: the Numbers, RxISK. August 17, 2015. <https://rxisk.org/antidepressants-and-violence-the-numbers/> [2022 [cited 2022 June 4]; Available from: URL:<https://rxisk.org/antidepressants-and-violence-the-numbers/>
215. Levenson CW. Zinc: The new antidepressant? *Nutr Rev* 2006; 64:39-42.
216. Nowak G, Szewczyk B, Pilc A. Zinc and depression. An update. *Pharmacological Reports* 2005; 57:713-718.
217. Cereda G, Ciappolino V, Boscutti A, Cantu F, Enrico P, Oldani L. Zinc as a neuroprotective nutrient for COVID-19-related neuropsychiatric manifestations: A literature review. *Adv Nutr* 2022; 13:66-79.
218. Ahmed A, Ghit A, Houjak A, Elkazzaz M. Role of zinc and zinc ionophores in brain health and depression especially during the COVID-19 pandemic. In: Palmero S, Olivier B, editors. *COVID-19 Pandemic, mental health and neuroscience- New Scenarios for understanding and treatment*. IntechOpen; 2022.
219. Ranjbar E, Kasaei MS, Mohammad-Shirazi M, Shams J, Mostafavi SA. Effects of zinc supplementation in patients with major depression: A randomized clinical trial. *Iranian J Psychiatry* 2013; 8:73-79.
220. Liu S, Sheng J, Li B, Zhang X. Recent advances in non-invasive brain stimulation for major depressive disorder. *Frontiers in Human Neuroscience* 2017; 11:526.
221. Brononi AR, Sampaio-Junior B, Moffa AH, Aparicio L, Gordon P, Klein I et al. Noninvasive brain stimulation in psychiatric disorders: a primer. *Brazilian Journal of Psychiatry* 2019; 4:70-81.
222. Dunlop K, Hanlon CA, Downar J. Noninvasive brain stimulation treatments for addiction and major depression. *Ann New York Acad Sci* 2017; 1394:31-54.
223. Mutz J, Edgumbe DR, Brunoni AR, Fu CH. Efficacy and acceptability of non-invasive brain stimulation for the treatment of adult unipolar and bipolar depression: A systematic review and meta-analysis of randomised sham-controlled trials. *Neuroscience and Biobehavioral Reviews* 2018; 92:291-303.
224. McClure D, Greenman SC, Koppulu SS, Varvara M, Yaseen ZS, Galynker II. A pilot study of safety and efficacy of cranial electrotherapy stimulation in treatment of bipolar II depression. *J Nerv Ment Dis* 2015; 203:827-835.

225. Wang YH, Li SA, Huang CH, Su HH, Chen YH. Sirt1 activation by post-ischemic treatment with lumbrokinase protects against myocardial ischemia-reperfusion injury. *Frontiers in Pharmacology* 2018; 9:636.
226. Yan XM, Kim CH, Lee CK, Shin JS, Cho IH. Intestinal absorption of fibrinolytic and proteolytic lumbrokinase extracted from earthworm, *Eisenia andrei*. *Korean J Physiol Pharmacol* 2010; 14:71-75.
227. Keihanian F, Saeidinia A, Bagheri RK, Johnston TP, Sahebkar A. Curcumin, hemostasis, thrombosis, and coagulation. *J Cell Physiol* 2018; 233:4497-4511.
228. Jacob A, Wu R, Zhou M, Wang P. Mechanism of the anti-inflammatory effect of Curcumin: PPAR-gamma activation. *PPAR Research* 2007; 2007:89369.
229. Kakavas S, Karayiannis D, Mastora Z. The complex interplay between immunonutrition, mast cells, and histamine signaling in COVID-19. *Nutrients* 2021; 13:3458.
230. Kunnumakkara AB, Harsha C, Banik K, Vikkurthi R, Sailo BL, Bordoloi D. Is curcumin bioavailability a problem in humans: Lessons from clinical trials. *Expert Opinion on Drug Metabolism & Toxicology* 2019; 15:705-733.
231. Moballegh Nasery M, Abadi B, Poormoghadam D, Zarrabi A, Keyhanvar P, Tavakol S et al. Curcumin delivery mediated by bio-based nanoparticles: A review. *Molecules* 2020; 25:689.
232. Valizadeh H, Danshina S, Gencer MZ, Ammari A, Sadeghi A, Aslani S. Nano-curcumin therapy, a promising method in modulating inflammatory cytokines in COVID-19 patients. *International Immunopharmacology* 2020; 89:107088.
233. Ahmadi R, Salari S, Reihani H, Eslami S. Oral nano-curcumin formulation efficacy in the management of mild to moderate outpatient COVID-19: A randomized triple-blind placebo-controlled clinical trial. *Food Science & Nutrition* 2021; 9:4068-4075.
234. Rahimi HR, Nedaeinia R, Shamloo AS, Nikdoust S. Novel delivery system for natural products: Nano-curcumin formulations. *AJP* 2016; 6:383.
235. Pretorius E, Venter C, Laubshder G, Kotze M, Moremi K. Combined triple treatment of fibrin amyloid microclots and platelet pathology in individuals with long COVID/Post -acute sequelae of COVID-19 (PASC) can resolve their persistent symptoms. *Research Square* 2021.
236. Ng WK, Rosenblatt Y, Brock GB, O'Gorman DB, Gan BS. Phosphodiesterase inhibitors in vascular ischemia: A case report and review of their use in ischemic conditions. *Can J Plast Surg* 2010; 18:e5-e9.
237. Usami O, Saitoh H, Ashino Y, Hattori T. Acyclovir reduces the duration of fever in patients with infectious mononucleosis-like illness. *Tohoku J Experi Med* 2013; 229:137-142.
238. Verma D, Thompson J, Swaminathan S. Spironolactone blocks Epstein-Barr virus production by inhibiting EBV SM protein function. *PNAS* 2016; 113:3609-3614.

239. Griffith RS, Wlash DE, Myrmel KH, Thompson RW. Success of L-Lysine therapy in frequently recurrent Herpes simplex infection. Treatment and prophylaxis. *Dermatologica* 1987; 175:183-190.
240. Griffith RS, Norins AL, Kagan C. A multicentered study of Lysine therapy in Herpes simplex infection. *Dermatologica* 1978; 156:257-267.
241. Andreu S, Ripa I, Bello-Morales R, Lopez-Guerrero JA. Valproic acid and its amidic derivatives as new antivirals against Alphaherpesviruses. *Viruses* 2020; 12:1356.
242. Gorres KL, Daigle D, Mohanram S, Mcinerney GE, Lyons DE. Valpromide inhibits Itic cycle reactivation of Epstein-Barr Virus. *mBio* 2016; 7:e00113-e00116.
243. Ornaghi S, Davis JN, Gorres KL, Miller G, Paidas MJ. Mood stabilizers inhibit cytomegalovirus infection. *Virology* 2016; 499:121-135.
244. Berg K, Bolt G, Andersen H, Owen TC. Zinc potentiates the antiviral action of human IFN-alpha tenfold. *J Interferon Cytokine Res* 2001; 21:471-474.
245. Skalny AV, Rink L, Ajsuvakova OP, Aschner M, Gritsenko VA. Zinc and respiratory tract infections: Perspectives for COVID-19. *Int J Mol Med* 2020; 46:17-26.
246. Dabbagh-Bazarbachi H, Clergeaud G, Quesada IM, Ortiz M, O'Sullivan CK. Zinc ionophore activity of Quercetin and Epigallocatechin-gallate: From Hepa 1-6 cells to a liposome model. *J Agric Food Chem* 2014; 62:8085-8093.
247. Langguth B. Treatment of tinnitus. *Curr Opin Otolaryngol Head Neck Surg* 2015; 23:361-368.
248. Langguth B. Pharmacological approaches to the treatment of tinnitus. *Drug Discovery Today* 2010; 15:300-305.
249. Langguth B, Elgoyhen AB, Cederroth CR. Therapeutic approaches to the treatment of tinnitus. *Ann Rev Pharmacol Toxicol* 2019; 59:291-313.
250. MartinezDevesda P, Waddell A, Perera R, Theodoulou M. Cognitive behavioral therapy for tinnitus (Review). *Cochrane Database of Syst Rev* 2007;(CD005233).
251. Sullivan M, Katon W, Russo J, Dobie R, Sakai C. A randomized trial of nortriptyline for severe chronic tinnitus effects on depression, disability, and tinnitus symptoms. *Arch Intern Med* 1993; 153:2251-2259.
252. Bayar N, Boke B, Turan E, Belgin E. Efficacy of amitriptyline in the treatment of subjective tinnitus. *Journal of Otolaryngology* 2001; 30:300-303.
253. Zoger S, Svedlund J, Holgers KM. The effects of sertraline on severe tinnitus suffering - A randomized, double-blind, placebo-controlled study. *J Clin Psychopharmacology* 2006; 26:32-39.
254. Bahmad FM, Venosa AR, Oliveira CA. Benzodiazepines and GABAergics in treating severe disabling tinnitus of predominantly cochlear origin. *12* 2006;(140):144.

255. Hosseinzadeh A, Kamrava SK, Moore BC, Reiter RJ, Ghaznavi HK. Molecular aspects of melatonin treatment in tinnitus: A review. *Current Drug Targets* 2019; 20:1112-1128.
256. Azevedo AA, Figueirido rR, Elgoyhen AB, Langguth B, Schlee W. Tinnitus treatment with oxytocin: A pilot study. *Front Neurol* 2017; 8:494.
257. Chen JJ, Zeng BY, Lui CC, Chen TY, Chen YW, Tseng PT. Pfizer-BioNTech COVID-19 vaccine-associated tinnitus and treatment with transcranial magnetic stimulation. *QJM* 2022.
258. Chen JJ, Zeng BS, Wu CN, Stubbs B, Carvalho AF, Su KP. Association of central noninvasive brain stimulation interventions with efficacy and safety in tinnitus management. A meta-analysis. *JAMA Otolaryngol Head Neck Surg* 2020; 146:801-809.
259. Han AY, Mukdad L, Long JL, Lopez IA. Anosmia in COVID-19: Mechanisms and significance. *Chemical senses* 2020; 45:423-428.
260. Boesveldt S, Postma EM, Boak D, Schopf V, Martens J, Duffy VB. Anosmia - A clinical review. *Chemical senses* 2017; 42:513-523.
261. Lee MR, Wehring HJ, McMahon RP, Cascella N, Liu F, Bellack A et al. Effects of adjunctive intranasal oxytocin on olfactory identification and clinical symptoms in schizophrenia: Results from a randomized double blind placebo controlled pilot study. *Schizophr Ews* 2013; 145:110-115.
262. Sorokowaka A, Drechsler E, Karwowski M, Hummel T. Effects of olfactory training: a meta-analysis. *Rhinology* 2017; 55:17-26.
263. Rashid RA, Zgair A, Al-Ani R. Effect of nasal corticosteroid in the treatment of anosmia due to COVID-19: A randomised double-blind placebo-controlled study. *American Journal of Otolaryngology-Head and Neck Medicine and Surgery* 2021; 42:103033.
264. Weng Z, Patel AB, Panagiotidou S, Theoharides TC. The novel flavone tetramethoxyluteolin is a potent inhibitor of human mast cells. *J Allergy Clin Immunol* 2015; 135:1044-1052.
265. Patel AB, Theoharides TC. Methoxyluteolin inhibits neuropeptide-stimulated proinflammatory mediator release via mTOR activation from human mast cells. *J Pharmacol Exp Ther* 2017; 361:462-471.
266. Theoharides TC. COVID-19, pulmonary mast cells, cytokine storms, and beneficial actions of luteolin. *Biofactors* 2020; 46:306-308.
267. Theoharides TT, Cholevas C, Polyzoidis K, Poliotis A. Long-COVID syndrome-associated brain fog and chemofog: Luteolin to the rescue. *Biofactors* 2021; 47:232-241.
268. Afrin LB, Weinstock LB, Molderings GJ. COVID-19 hyperinflammation and post-Covid-19 illness may be rooted in mast cell activation syndrome. *Int J Infect Dis* 2020.

269. Klooker TK, Braak B, Koopman KE, Welting O, Wouters MM, Schemann M. The mast cell stabiliser ketotifen decreases visceral hypersensitivity and improves intestinal symptoms in patients with irritable bowel syndrome. *Gut* 2010; 59:1213-1221.
270. Wang J, Wang Y, Zhou H, Gu W, Wang X, Yang J. Clinical efficacy and safety of ketotifen in treating irritable bowel syndrome with diarrhea. *Eur J Gastroenterol Hepatol* 2020; 32:706-712.
271. Nguyen B, Tosti A. Alopecia in COVID-19: Systematic review and meta-analysis. *JAAD International* 2022; 7:67-77.
272. Darwin E, Hirt PA, Fertig R, Doliner B, Delcanto G. Alopecia areata: Review of epidemiology, clinical features, pathogenesis, and new treatment options. *International Journal of Trichology* 2018; 10:51-60.
273. Wikramanayake TC, Villasante AC, Mauro LM, Perez CI, Jimenez JJ. Prevention and treatment of alopecia areata with quercetin in the C3H/HeJ mouse model. *Cell Stress and Chaperones* 2012; 17:267-274.
274. Nichols AJ, Hughs OB, Canazza A, Zaiac M. An open-label evaluator blinded study of the efficacy and safety of a new nutritional supplement in androgenic alopecia: A pilot study. *Journal of Clinical and Aesthetic Dermatology* 2017; 10:52.
275. Karatas F, Sahin S, sever AR, Altundag K. Management of hair loss associated with endocrine therapy in patients with breast cancer: an overview. *SpringerPlus* 2016; 5:585.
276. Harvey CJ. Combined diet and supplementation therapy resolves alopecia areata in paediatric patient: A case study. *Cureus* 2020; 12:e11371.
277. Stoehr JR, Choi JN, Colavincenzo M, Vanderweil S. Off-label use of topical minoxidil in alopecia: A review. *Am J Clin Dermatol* 2019; 20:237-250.
278. Gupta AK, Venkataraman M, Talukder M, Bamimore MA. Finasteride for hair loss: a review. *Journal of Dermatological Treatment* 2021.
279. Geerts M, de Greef BT, Sopacua M, Faber CG. Intravenous immunoglobulin therapy in patients with painful idiopathic small fiber neuropathy. *Neurology* 2022; 96:e2534-e2545.