An Approach to the Management of Post-Vaccine Syndrome

I-RECOVER℠
POST-VACCINE TREATMENT

Disclosure

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

Contributors

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

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Definition

Although no official definition exists for post-COVID-vaccine syndrome, a temporal correlation between a patient receiving a COVID-19 vaccine and beginning or worsening of 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 16, 2022, 815,385 adverse events have been reported in the United States alone following COVID-19 vaccination. In addition, over 5,309 cases of myocarditis, 151,796 serious adverse events, and 14,613 deaths have been recorded in the U.S. Vaccine Adverse Event Reporting System (VAERS) following COVID-19 vaccination. Note that the VAERS database is limited by underreporting, by a factor of at least 30-fold. [2]

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 results of an acute type I IgE mediated hypersensitivity reaction. The type I response may be due to preformed antibodies against mRNA, polyethylene glycol [7] or other components of the nano-lipid particle.
- 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. [8]
- The subacute and chronic myocarditis is likely the result of a spike protein-induced inflammatory response mediated by pericytes and macrophages. [9,10]
- 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.

Due to molecular mimicry with the spike protein, a diverse spectrum of autoantibodies is produced. [11-20] These autoantibodies are the likely cause of Guillain-Barré Syndrome (GBS), transverse myelitis, immune thrombocytopenia, and Small Fiber Neuropathy (SFN)/Autonomic neuropathy. [21-28]

Many of these antibodies are directed against G-protein coupled cell membrane receptors. [17,19] 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 micro clots (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. [29,30] However, by definition MCAS has no identifiable causes, is not caused by allergen specific IgE and has no detectable clonal expansion of mast cells. [29]

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. [31-33]

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.
- **mRNA load and quantity of spike protein produced**: This may be linked to specific vaccine lots that contain a higher concentration of mRNA. [1]
- **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. [34] 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 with methylenetetrahydrofolate reductase (MTHFR) gene mutations and Ehlers-Danlos type syndromes may be at an increased risk, as well as those with deficiencies of nutrients such as Vitamin B12, Vitamin D and magnesium.

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.
- Similarly, 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. We recommend a number of simple, basic screening tests that should be repeated, as clinically indicated, every 4 to 6 months. Remember the dictum: Only do a test if the result will change your treatment plan.
- Hyperbaric oxygen therapy (HBOT) should be considered in cases of severe neurological injury and in patients showing a rapid downhill course (see below).
- Patients should avoid unscientific and poorly validated "Spike Protein Detox" programs.

Baseline Testing

- CBC with differential and platelet count
- Standard blood chemistries, including liver function tests
- D-Dimer—as a marker of clotting activation)
- 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
- HbA1C—Vaccine-injured patients are at an increased risk of developing diabetes.
- Troponin, pro-BNP, Galectin-3, and ST2—to exclude cardiac disease.
- CMV, EBV, 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/)
- 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. [29]
- 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, [17,19] ACE-2, [35] 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. [36-42] Intermittent fasting likely has an important role in promoting the breakdown and elimination of the spike protein.
- **Ivermectin; 0.2-0.3 mg/kg, daily for up to 4-6 weeks**. Ivermectin has potent anti-inflammatory properties. [43-45] It also binds to the spike protein, aiding in the elimination by the host. [46-48] It is likely that ivermectin and intermittent fasting act synergistically to rid the body of the spike protein. A trial of ivermectin should be considered as first line therapy. It appears that patients can be grouped into two categories: i) ivermectin responders and ii) ivermectin non-responders. This distinction is important, as the latter group are more difficult to treat and require more aggressive therapy.
- **Low dose naltrexone (LDN);** LDN has been demonstrated to have anti-inflammatory, analgesic and neuromodulating properties. [49,50] 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. [51-55] 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. [56-60] 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.
- **Quercetin;** 250-500 mg/day (or mixed flavonoids). Flavonoids have broad spectrum anti-inflammatory properties, inhibit mast cells, [61-65] and have been demonstrated to reduce neuroinflammation. [66] Due to the possible drug interaction between quercetin and ivermectin (see below) 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. [67] 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.
- **Nigella Sativa;** 200-500 mg twice daily. [68-71] 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. [72] Furthermore, two cases of serotonin syndrome have been reported in patients taking Nigella Sativa who underwent general anesthesia (probable interaction with opiates). [73]
- **Probiotics/prebiotics**; Patients with post-vaccine syndrome classically have a severe dysbiosis with loss of Bifidobacterium. [74-76] Kefir is a highly recommended nutritional supplement high in probiotics. [77] Suggested probiotics include Megasporebiotic (Microbiome labs) and TrueBifidoPro (US Enzymes).
- **Magnesium**; 500 mg/day.
- **Omega-3 fatty acids**: Vascepa, Lovaza or DHA/EPA; 4 g/day. Omega-3 fatty acids play an important role in the resolution of inflammation by inducing resolvin production. [78,79]

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. [80-84] With long term usage, the dose should be reduced (100 or 150mg/day) in patients weighing less than 61 kg (135 lbs).

- **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. [85-90] Wean IV Vitamin C as tolerated.
- **Fluvoxamine**; Start on a low dose of 12.5 mg/day and increase slowly as tolerated.
- **"Mitochondrial energy optimizer"** with pyrroloquinoline quinone (e.g., Life Extension Energy Optimizer or ATP 360®). [91-93]
- **N-acetyl cysteine (NAC)**; 600-1500 mg/day. [94-96]
- **Sulforaphane (broccoli extract)**; 400 mcg/day. [97-99]
- **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** [100] **and psychological support** may help improve patients overall well-being and mental health. [101] Suicide is a real problem in the vaccine-injured patient. Support groups and consultation with mental health professionals is important.
- **Tai Chi**; Tai Chi is a health-promoting form of traditional Chinese martial art, shown to be beneficial for preventing and treating diseases including long COVID. [102,103] It should be noted that long COVID is characterized by severe post-exertional fatigue and/or worsening of symptomology, therefore patients should be counseled to moderate exertion, increasing slowly only as tolerated. [104]

Third Line Therapy

- **Hyperbaric oxygen therapy** (HBOT) [105-113]; 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 life-saving benefits have been reported anecdotally. This therapy is limited by logistical issues and cost.

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. [115-122] Kiprov, et. al. have published a case report of a dramatic clinical improvement in a patient with long COVID. [123] 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. [124] 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. [114]
- **Valproic acid** [125,126]; Depakote, 250mg 2-3 times daily. Valproic acid has anti-inflammatory effects and polarizes macrophages towards a M2 phenotype. [127] HDAC inhibitors are being studied for neural regeneration. In addition, valproic acid has important anticoagulant and anti-platelet effects. [128] Valproic acid may be helpful for neurological symptoms.
- **Sildenafil** with or without L-arginine-L-Citrulline [129-134]; 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.
- **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 flavonoid combinations is unknown. [135]
- **C60 or C60 fullerenes** [136,137]; 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) [138,139]; 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
- A trial of hyperbaric oxygen therapy (HBOT)
- It should be noted that the diagnosis of small fiber neuropathy/autonomic neuropathy is a clinical diagnosis. [21-28] 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.

Generalized Neurologic Symptoms/Injuries/"Brain Fog"/Fatigue

- LDN appears to play a pivotal role in treatment of many neurological symptoms
- 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.
- Nigella Sativa; 200-500 mg twice daily.
- Valproic acid and pentoxifylline may be of value in these patients.
- These symptoms may be mediated by Mast Cell Activation Syndrome (MCAS); see specific treatment below.

Patients with an 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). [140] Lumbrokinase appears to be well absorbed from the GI tract. [141]
- Turmeric (Curcumin) 500 mg BID. Curcumin has anticoagulant, antiplatelet and fibrinolytic properties. [142]
- Triple anticoagulation should be considered in select patients. [143] 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. [124,144]

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

- L-Lysine; 1000 mg twice daily [145,146]
- Valtrex; 500-1000 mg twice daily for 7-10 days

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. [147]
- 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: [147-149]
    - Cognitive behavioral therapy [150]
    - Specialized therapy including tinnitus retraining therapy, hearing aids, sound therapy, auditory perceptual training and repetitive transcranial magnetic stimulation. [147]
    - 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. [151,152] In addition, the SSRI sertraline has shown some efficacy. [153]
        - Clonazepam and or other benzodiazepines. These drugs may provide temporary relief, however, due to issue of dependence, long term use is not recommended. [154]
        - Melatonin slow release 2-6 mg at bedtime. [155]

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 and those with features of Mast Cell Activation Syndrome (MCAS)

- The novel flavonoid lutein is reported to be a potent mast cell inhibitor. [61,62,64,65] Lutein 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. [156,157]
- 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. [158]

- Montelukast 10 mg/day. Caution as may cause depression is some patients. The efficacy of montelukast as a "mast cell stabilizer' has been questioned. [29]
- 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.

IVIG treatment (Intravenous immunoglobulin treatment)

- Generally, treatment with IVIG is not recommended.
- 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 2to 3 weeks. Other patients report no benefit, while some appear worsened. Due to the presence of non-neutralizing anti-SARS-CoV-2 antibodies, 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 a RCT that enrolled patients with small fiber neuropathy. [159]
- 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.

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