Pre- and Post-Vaccine Support Considerations*

Introduction

I got the opportunity to have a podcast with Ben this week where we discussed the implications of the COVID vaccination. In the podcast we discussed strategies we can use to optimize the body before the vaccination as well as strategies that can be used if somebody had a significant immune flair after the vaccination. This is with the caveat that we don't turn the immune response down too much. We also briefly discussed some of the medications that are used for prophylaxis, monoclonal antibodies that are used in some rare circumstances for prophylaxis, and some of the medications being used for both prophylaxis and therapy for COVID. When I mentioned that we had a list of some strategies we are using and we've been handing out for patients, Ben asked me if I could make a PDF of it. We ended up dictating all off our initial thoughts that came to mind and unfortunately that turned out to be 20 pages, so here you go.

It is imperative to note that mild-to-moderate flu-like symptoms are a normal and expected part of a healthy immune response to vaccination. Due to a lack of scientific research showing the effect of these strategies on vaccine effectiveness, if any of them are used after vaccination, they should be used with caution, and only when side effects are severe or inappropriately persistent (e.g., greater than 10 days).

This places a person trying to get a vaccine a little bit between a rock and a hard place. On the one hand, we're trying to support the immune system so that it is in the most calm and balanced state before receiving the vaccine, but on the other hand we do not want to blunt the immune response in a way that reduces immunity to COVID (that is, by suppressing antibody production). Thus, these are very nuanced judgments that we have to make about how to support the immune system before and after a vaccine: if we optimally balance immune activity before vaccination, we anticipate someone will have an appropriate immune response to the vaccine.

If we take too much to blunt the immune response after the vaccine, we risk reducing antibody production, which negatively affects positive immunity to a highly contagious virus. This is particularly important in immunocompromised patients, who may make less antibodies. On the other hand, some individuals may be predisposed to having an overactive inflammatory response, which can lead to negative and persistent immune activation and the symptoms that come with it.

Therefore, this requires a thoughtful and cautious approach, and we think that the best case scenario is that you are guided by a qualified healthcare practitioner who has experience in this arena and is close to you, who can support you and help you make judgment calls so that you

can get prepared to receive the vaccine, and to manage some of the reactions that we sometimes see occur after the vaccine.

As a result, we put this document together with the doctors in our office to help support our patients. We realized that after we did the podcast that there is significantly more content about preparing for a vaccine that we could do in a short podcast. As a result, we put together this guide that we hope will be a starting point for a conversation with a healthcare professional who knows you and can help guide you through the complex journey of making a decision to get vaccinated and going through it in a healthy and safe way.

During the podcast, I took a fairly strong pro-vaccine stance. We are in regular contact with anesthesiologists and ICU doctors who are taking care of very sick patients all over the world with COVID and it became clear over the last year that the vaccinated population is less likely to have a catastrophic COVID experience. Additionally, if a large percentage of the population doesn't get vaccinated, there is a possibility it will have some very negative impactful ramifications on the health and wellness of our society worldwide.

That being said, I and the doctors in our practice have dedicated ourselves to taking care of patients with complex immune conditions. Collectively, we have taken care of thousands of patients who feel they've had vaccine injuries. I have listened to people tell me that after a vaccine, they've had new problems. I've also had patients whose presenting complaint was that they had a new problem after receiving a COVID vaccine.

Conversely, every day we take care of long-haul COVID patients, and our general consensus is that the probability of a negative long-term consequence from COVID infection is in the ballpark of 10- to 100-times more than that of a reaction to the vaccine. We have also found that most people with vaccine reactions recover relatively quickly and are easier to treat than many of those struggling with long-haul COVID. If there was one thing that I'd like you to hear, is that although there may be problems, in general we are seeing almost everyone do well with vaccinations. I say that as a doctor who takes care of patients with complex illness, and to reassure you that we are having patients have safe experiences as they go through this challenging journey.

We're now beginning to see patients on a weekly basis via telemedicine who are getting COVID for the second, third, or even fourth time. Though this is likely due in part to the existence of newer, more contagious variants, recent research suggests that vaccinated patients are dramatically less likely to become very sick from the Delta variant.

Although we are seeing some breakthrough cases in vaccinated individuals, it's relatively easy to deal with, and we haven't seen any of these patients remotely near needing to go to the hospital.

Additionally, epidemiologically, there is concern that having a large number of unvaccinated individuals increases the likelihood of forming new variants. This is because the virus replicates

more in unvaccinated individuals because the lack of antibodies means the immune system is not able to keep the virus in check. More replication cycles means more opportunities for “errors” in synthesis, which is another way of saying that the virus just mutated.

We understand that there’s a great amount of political, social, and professional pressure. Employers are beginning to mandate vaccinations, and doctors are being pushed into getting vaccinated. It’s tricky.

On the one hand, if you think a treatment is going to help you, the placebo effect can make it more positively impactful. On the other hand, if you are very afraid of a treatment, it may lead to a more negative outcome - that’s called the nocebo effect.

I delved into the science of these recent vaccines, and I’m relatively encouraged that the mRNA vaccines don’t last that long; there is more information on the mRNA vaccines below. They create an immune response that can lead to positive immunity but without many persistent negative effects in the body. We have seen some patients with long haul COVID who have gotten better after the vaccine.

They say that the answer to every anesthesia oral board exam begins with the statement, “It depends.” I don’t think that there are any hard and fast rules that can necessarily be applied for judgment calls about how best to take care of oneself regarding this topic. Social, cultural, religious, political, and biochemical aspects all come into play. A person’s infectious disease history, genetics, and other factors also play significant roles.

No matter what decision you make, we are rooting for you. The ideas that are discussed in this document may be helpful in optimizing wellness and may be helpful in preparing your body before or after a vaccine.

This is still very early in the game. We’ve been supporting pre- and post-vaccinated individuals for less than a year - it’s very early, and over the arc of the next few months, we’re going to learn a lot more than we are even beginning to indicate here.

Therefore, we’re going to continue to update this document with anything that we learn. If you have found something that works or if you disagree with any of the science that we’ve discussed, we’d love to hear from you, and we are open to constructive dialogue and to adapting the information that we’re sharing, based on the rapidly changing landscape of this worldwide pandemic using an evidence- and clinically-based approach.

Statement about Ivermectin and Hydroxychloroquine

During the podcast, we discussed the fact that there is some vaccine hesitancy based upon the idea that there are some alternative treatments for COVID. My general stance is that there are a handful of supportive integrative approaches that are being used for COVID. In broad terms, my clinical sense from taking care of patients is that by far the best prophylaxis against COVID is

the COVID vaccine. There are some patients that have used ivermectin for prophylaxis. We haven't found great data supporting this.

As an anecdote, ivermectin is also something many patients have been using to treat COVID. There have certainly been a lot of positive case reports shared to me by other doctors. Our clinical experience and our review of the literature of ivermectin to actively treat COVID paints a somewhat unclear picture. The scientific evidence is not very strong. A recent Cochrane review meta-analysis yielded very low- to low-certainty evidence about the safety and efficacy of ivermectin for COVID. We have seen it be empirically helpful in some cases, however these were not controlled clinical trials and many other therapeutic factors were individualized.

Another medicine that came out early as a possible prophylactic and therapeutic agent is hydroxychloroquine. Hydroxychloroquine data has also been somewhat lacking. In addition, hydroxychloroquine has some fairly serious potential side effects from the perspective of cardiac systems. Our thought process is that hydroxychloroquine involves somewhat of a risk for probably not a very high reward, in terms of what the data is showing, both for treatment and for prophylaxis.

During the podcast I was somewhat dismissive of ivermectin. I don't want to be 100% dismissive about ivermectin because I have talked to quite a few patients who have had some benefits from it, but my concerns are that, (1) it is unproven and per Uptodate, "The National Institutes of Health's COVID-19 guidelines panel continue to indicate that there are insufficient data to recommend for or against the use of ivermectin for the treatment of COVID-19 and that results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance." (2) people are using veterinary formulations of the medication by bypassing the advice and guidance from their healthcare practitioners(3) there is a perception that taking ivermectin provides protection from the virus, but our sense of the data is that any help that the medication may offer is much less than what the public thinks it offers. There was a sense early on in the pandemic that hydroxychloroquine was going to be great for prophylaxis as well. In general, this has not really turned out to be the case. We would categorize both these medications as mildly prophylactic, but not anywhere close to the prophylactic benefit of vaccination.

During the podcast we also mentioned monoclonal antibodies, which is a treatment that has been met with some very positive data in the last 6 months. Monoclonal antibodies are antibodies that mimic what your body would make during an actual infection. They recognize and bind to the spike protein on the outer shell of the virus and prevent the virus from entering our cells.

The monoclonal antibody data that has come out has been robust, and monoclonal antibody treatment is becoming increasingly more available. In fact, most urgent care centers are beginning to offer it. This podcast and this document was not meant to delve deeply into treatment options for COVID, however some medications which are being used for prophylaxis are also used for treatment. The monoclonal antibodies are primarily being used for treatment of

COVID, however in some rare cases it's also being used for prophylaxis. We would say in broad terms that there are probably not any great prophylactic approaches for COVID other than vaccination. Monoclonal antibodies have no place in the pre and post vaccine intervention conversation. They will also have an extremely limited role for prophylaxis and likely in immunocompromised patients only. However, they are evolving to have a significant role in the treatment of symptomatic patients who COVID-19.

Examination of COVID Vaccines

There's a point in the podcast where we talk about the mRNA vaccines. These are the Pfizer-BioNTech and Moderna vaccines. The way they work is that they contain messenger RNA that are instructions for our cells to print a protein. The protein printed is a spike protein that gets put on the outside of a cell and generates an immune response. Due to the relative instability of the mRNA vaccine it is wrapped in a lipid casing that goes into the body and is absorbed by cells that print the spike protein. It only exists in the body for a few weeks and it is broken down 100%. Cells with spike proteins end up being cleared and it leads to an immune response. That immune response leads to generation of antibodies and also leads to the generation of some cells (such as plasma cells that are long lived cells that may live within the body and generate a future immune response to insult in the future).

The other vaccines are based on the adenovirus platform. The two most common vaccines for this platform are the AstraZeneca and the Johnson and Johnson vaccine. Those vaccines involve viral DNA that is put into an adenovirus which is used to infect your cells and put the viral DNA into your DNA and cause your DNA to make mRNA which would make the spike protein. This is a traditional vaccine platform that's been used longer than the mRNA platform.

From a certain perspective, there may be benefits to both. We have leaned towards the mRNA vaccines. One point to consider is that with the mRNA vaccines, you get two chances to mount an immune response. Each one of these chances prepares the body to deal with the virus. Most people we talk to have some reaction to the first dose, but a bigger reaction to the second dose. This makes sense. The first dose is priming the patient for the second dose.

Regarding the adenovirus vaccines, patients have one shot to make an immune response. As a result, it is a very nuanced decision that needs to be made between the doctor and the patient in terms of doing anything to regulate immune response down from the vaccine because it could lead to a lower immune response and less immunity from the vaccine. This will be the case with vaccines on either platform. That being said, if an immune reaction is happening for multiple days and begins to accelerate, our goal in putting this document together is to create some awareness of possible integrative strategies that can be used to support patients through this while not blunting the immune response so the vaccine is less effective.

These are supportive things patients can do themselves and this is a judgement call because there's not going to be strong data on many if any of these modalities because we are so early

in the pandemic, therefore our goal is to create some awareness on what people are or may be doing, and to create a conversation that we can begin to track and follow and share information in an open way with people as they are making life and death decisions that have broad implications for themselves, their families, and society at large.

We have seen some patients that have already had COVID have a strong reaction to the first mRNA vaccine dose. This can depend on how recently someone had COVID. There is some interesting research related to this. A recent large Israeli study showed that immunity to the Delta variant was greater following a natural infection than that following two doses of the Pfizer-BioNTech vaccine. However, they also found that those who previously had COVID and then received a single dose of the Pfizer-BioNTech vaccine had better immunity to re-infection than those who were previously infected but remained unvaccinated. Some scientists are fairly confident that one dose of an mRNA vaccine is enough for people who were previously infected. Some European countries are giving just one dose to people who had COVID previously.

That being said, we want to make it very clear that risking infection by remaining unvaccinated in order to seek out natural immunity is not something we advise, and may not be worth the risks, as research continues to demonstrate significantly higher rates of severe infection and death among unvaccinated vs. vaccinated individuals.

One very important topic that we are actively paying attention to is timing of when to get a vaccine. We have many patients who are in extremely complicated medical conditions who are trying to navigate their way through a complex medical course in addition to managing COVID prophylaxis through the pandemic. These are generally case by case judgements and we are going to add to this segment of the conversation. Some of the topics that we consider relevant include pregnancy, Lyme disease, autoimmune disease, and traumatic brain injury. In terms of pregnancy, there are a lot of factors at play and we do not have all the answers yet. The CDC recommends vaccination during pregnancy as COVID has been seen to transfer from mothers to infants during pregnancy.

Our decision to tackle the vaccine conversation on the podcast and to put this document up was not made lightly because we knew it would be met with a fair amount of controversy. We are well aware that there have been patients that have had vaccine problems for decades and we are very empathetic to their plight. In fact many of these patients have seen us for one type of therapy or another. We are also aware that, from a social and a deterministic perspective, a lot of people feel that the choice about what to do with their body is the most important choice they have to make. It feels like quite an insult to them when their medical freedom is compromised.

That being said, we have also found that COVID is a real and profound problem. We have had deep consultation from the beginning of the pandemic with patients from all over the world who have had everywhere from mild to profoundly debilitating illness. Some of those that have profoundly debilitating illness will continue to have lasting health consequences for the rest of their lives.

The optimal treatment course is not known but I think we have been learning with our patients and with the community at large how to cope with this in better and better ways. In this document we will discuss some of the approaches currently used for prophylaxis and we will talk a little bit about the data vaccines give from a prophylactic perspective. We will not go into any ideas about treating COVID because the consequences of that are potentially even higher than the COVID vaccines.

That being said, we welcome your comments, wisdom, and stories. We look forward to engaging in this conversation as we struggle to find an optimal way to work through this problem. In many cases, particularly in Western medicine, there is a sense of what is right and what is wrong or what is clinically indicated and what is not. We would like to have a perfect and complete answer that was 100% evidence-based that we could tell you but I don't think we know, no one probably does. This will be an evolving journey that we are on together.

We are taking a stance that the vaccines at this point seem to be helping and generating good data and that the vaccine complication rates seem to be an order of magnitude less than the COVID complication rate. That being said, it is early and we may find over the next weeks, months, and years to come that there are problems. However, at this point we have to use our best judgement to help make a decision and we have decided to take a stand and say we think this is the right thing to do and we know that in our best effort to save the many, a few people will be hurt along the way. Science is using your best ability in the moment to assess what is safe and effective and to always be willing to change that as new data is recorded.

Whole-Person Support:

- These are foundational ideas that we can all adapt as long-term wellness strategies.
- The concept of challenging the hygiene hypothesis vs. strengthening the terrain is key when talking about immune approaches
    - Many individuals are infected with pathogenic organisms and do not get long-standing/debilitating diseases, so understanding how to strengthen one's resilience and immune response is key.
- When aiming to reduce the likelihood of side effects, it is critical to have a baseline understanding of one's overall immunologic and toxic burdens. Current medications, past medical history, current illnesses, and clinical and laboratory evaluation of inflammatory markers, cardio-metabolic markers, vitamin D and other nutrient levels, vector-borne infections, opportunistic infections, mycotoxin and chemical toxin burdens, and genetic SNPs can each contribute to suboptimal immune dynamics.
- Adequate water intake with electrolytes to ensure optimal hydration status.
- Regular movement/exercise practices.

- High intake of antioxidant-rich foods.
- Sufficient sleep, generally at least 8 hours per night.
- Appropriate management of psycho-social stress.
- Our general perspective is that everything that can be done at this level to optimize wellness before the vaccine puts your immune system in the best possible place to receive the vaccine.

Hydrotherapy:

- Alternating hot and cold applications improve circulation of blood and lymph by means of inducing peripheral vasodilation and vasoconstriction, which supports delivery of nutrients to tissues and removal of waste products from tissues.
- This may be my favorite biohacking strategy. The first thing I do when I go to Ben Greenfield's house is jump in the sauna, then jump into the Morozko Forge ice bath.
- For those less acclimated to hot and cold, we end our showers with 30-60 seconds of cool-to-cold water as tolerated, working down gradually to colder temperatures.

Supplement Considerations:

- **Perhaps the most crucial concept when it comes to maintaining a healthy immune response (that is not over- or under-active) is balancing ReDox biology.** The ReDox system of the body is the complex way that antioxidants and oxidizing agents are utilized and recycled to help keep oxidative stress contained while still performing necessary cellular and immune functions. This ReDox balance is very delicate and nuanced, because in some cases you want an oxidative process to occur. In other cases, there is too much oxidation, and antioxidants (also known as reducing agents) are needed. Rather than try to control this ourselves, giving the body the building blocks it needs to maintain this balance on its own is the preferred approach. Individual agents are discussed in more detail in this document, but the basic foundations for ReDox balance are as follows:
    - Dietary omega-3 fatty acids and phospholipids (phosphatidylcholine and phosphatidylserine)
    - Mixed vitamin E tocopherols
    - Vitamin C
    - Glutathione

    - Co-factors involved in glutathione synthesis and recycling - vitamin B2, B3, B5, zinc, selenium, and magnesium.
    - Alpha lipoic acid and NAC can also be helpful in support glutathione production
- Some integrative medical providers have argued that these ReDox balancing agents are more important than any other immune modulating supplements, because they support the “terrain” of the body in the most fundamental way.

- **Mixed vitamin E tocopherols/tocotrienols**
    - Cell membrane protection, blood clot prevention, and lowering of blood viscosity
    - Pair with selenium and vitamin C to ensure better glutathione recycling

- **Liposomal Vitamin C**
    - Liposomal vitamin C is fat-soluble and can be more readily absorbed compared to standard oral vitamin C, especially if GI is impaired
    - Helps maintain antioxidant/redox balance and is involved in glutathione recycling (see discussion above)
    - Vitamin C can also be given intravenously. One common formulation of this is called a Myer’s cocktail (see IV therapy section below).
    - We’ve had many patients tell us that they’ve found oral vitamin C beneficial both before and after the vaccine

- **Vitamin A**
    - Upregulates Toll-like receptors in the GI tract which are critical for mounting an immune response
    - Upregulates secretory IgA along the mucosal surface – the surfaces of the respiratory and GI tracts are the first point of entry for a respiratory virus

- **Vitamin D3**
    - Modulates both the innate and adaptive immune responses
    - Ideal dosing and blood levels may depend on pre-existing medical conditions
    - Avoid high doses after vaccination, unless having a severe or inappropriately persistent inflammatory response

- **Vitamin B5**
    - Critical cofactor for NAT2-mediated histamine clearance, which is important in reducing the severity of mast cell activation reactions.
    - Mast cell activation is a constellation of symptoms related to a hyper-active allergy-type response. These symptoms tend to be common in individuals with chronic infections and environmental illness. More information about this condition is at the end of the document

- **Specialized Pro-Resolving Mediators (SPMs)**

    - These are a purified fish oil product, and tend to be more bioavailable and better absorbed than standard fish oils
    - Helps resolve an aberrant and persistent inflammatory response
    - Useful for mold sickness (also known as CIRS). We have seen these individuals trend toward being more hypersensitive due to dysregulated immune dynamics.
        - Individuals with mold toxicity cannot absorb fats very well and SPMs can help aid fat absorption
    - Use with caution if after vaccination, unless having a severe or inappropriately persistent inflammatory response

- **Combination binder product (activated charcoal, bentonite/zeolite clay, etc.)**
    - Helps remove chemical toxins and mycotoxins (from mold) from the re-absorption/recirculation cycle of bile so that they can be excreted from the body
    - GI detoxifying agents have been an important component of naturopathic medicine for over a century. This approach is based upon the theory that improving toxin removal from the GI tract reduces additional inflammatory activity and allows the immune system to better respond to the most immediate immune stimulus.
    - Must be taken at least 90-120 minutes away from food, medications, and other supplements, generally at night before sleep
    - If these cause constipation, reduce dose until tolerated
    - Our clinical experience suggests it can be helpful at mitigating side effects if taken immediately post-vaccine on an empty stomach

- **Homeopathic Thuja 30c and Arnica 30c**
    - Homeopathy is a system of medicine that has been practiced for hundreds of years. There are some homeopathic products that some patients have shared that have been helpful in their journey around vaccines.
    - Alternate Thuja 30c and Arnica 30c every 2-4 hours post-vaccine for arm pain and body aches, for up to 7 days.
    - In individuals too sensitive to supplements, consider more gentle lymphatic drainage homeopathics or NAET therapy, which is an allergy treatment technique that is a combination of acupressure and applied kinesiology.

Agarikon mushroom:

- **Curcumin/Turmeric:**
    - Derived from turmeric spice, a key ingredient in curry powder and in traditional Eastern diets
    - Popularized and often used for its anti-inflammatory properties, curcumin has also been demonstrated in research to modulate the immune system (including

activation of T cells and B cells, macrophages, neutrophils, NK cells, and dendritic cells).
    - It can reduce some of the pro-inflammatory cytokines induced by NF-kappaB
    - Dietary doses of curcumin have been shown to improve antibody responses, which may be a worthwhile consideration in the context of vaccination
    - We see curcumin helpful clinically for patients with overactive inflammatory responses
    - Use with caution if after vaccination, unless having a severe or inappropriately persistent inflammatory response

- **Grapefruit seed extract**
    - Improves blood vessel wall (endothelium) integrity
    - Broad-spectrum antimicrobial that can reduce additional immune activation from chronic infection or gastrointestinal dysbiosis

- **Melatonin**
    - Melatonin is a fairly profound antioxidant for the central nervous system. There are benefits and applications of both low-dose and high-dose melatonin. On the positive side, it may help to modulate immune responses. This has been a tool that some patients that we have talked to have used as a strategy both to help them sleep and to deal with central nervous system inflammation. Because high-dose melatonin may have the tendency to dampen an immune response, consult a healthcare practitioner about this, but of course that goes for everything in this document.
    - Turns down NLRP3-inflammasome activity to help modulate an overactive inflammatory response
    - Melatonin is also a zinc ionophore, which increase intracellular zinc uptake
    - Use with caution if after vaccination, unless having a severe or inappropriately persistent inflammatory response

- ***trans*-Resveratrol**
    - Helpful at stabilizing mast cells and reducing histamine-type responses
    - Neuroprotective and cardiovascular protective polyphenol
    - Resveratrol is also found in red wine

- **Astragalus**
    - Potent immune modulating herb that helps regulate the inflammatory response
    - Use with caution if after vaccination, unless having a severe or inappropriately persistent inflammatory response

- **Holy Basil**

    - Holy basil is an “adaptogenic” herb that helps modulate the hypothalamic-pituitary-adrenal axis, which can be helpful in prolonged states of physiologic and psycho-emotional stress.
        - Other adaptogenic herbs include rhodiola, eleuthero, ashwagandha, and schisandra
        - These may be beneficial in cases of persistent fatigue
    - Reduces MMP-9 and mast cell activity
    - Use with caution if after vaccination, unless having a severe or inappropriately persistent inflammatory response

- **Rhodiola**
    - Improves mitochondrial, immune, and neuro-endocrine function, has research supporting its use in altitude sickness/hypoxia
    - Use with caution if after vaccination, unless having a severe or inappropriately persistent inflammatory response

- **NMN/NR**
    - NMN stands for nicotinamide mononucleotide and NR stands for nicotinamide riboside, and these are both precursors to NAD that can be taken orally
    - These are two supplements that many of our patients use to help support their NAD levels

- **Colostrum/oral immunoglobulins:**
    - Bovine colostrum and oral immunoglobulins act as binders and can assist in regulating the gastrointestinal microbiome and local immune environment by removing immune-activating antigens and GI pathogens
    - There is also some research demonstrating that gut barrier function was improved by colostrum following damage by NSAIDs
    - We see these helpful clinically in our complex immune patients, especially when there is GI dysbiosis (microbiome imbalance) present

IV Nutritional Therapy:

- **Broad-spectrum IV micronutrient support**, including ascorbic acid (vitamin C), B vitamins, amino acids, and minerals can improve nutritional bioavailability and may help normalize cellular and inflammatory activity
    - These formulas may sometimes be referred to as “Myer’s cocktails”, although there are many variations of a Myer’s formula and many ways to formulate IV nutritional bags. Please refer to a healthcare professional who is certified to administer IV nutritional therapy for more information
    - Consider up to twice weekly

- **IV glutathione**

    - Repletes endogenous glutathione stores
    - For those unable to afford/access IV glutathione - NAC orally is a good and cheaper alternative
    - Consider being careful with glutathione - individuals who have difficulties with sulfur moieties may have difficulty processing glutathione. Incorporating the mineral molybdenum which can be helpful in aiding sulfur metabolism.
    - For patients who have never had glutathione, we always start with a lower dose

- **IV NAD+**
    - Repletes cellular NAD stores that deplete with aging and chronic disease, improving mitochondrial function
    - Inhibits PARP-1 and prevents pro-inflammatory cytokine overactivation
    - Dosage determines treatment frequency
    - Consider the individual's constitution/vitality to determine starting dose and dose escalation; also constitution will determine if IV is appropriate versus subcutaneous injection, topical cream, intranasal, or oral liposomal.
    - The subcutaneous injection can be done with an insulin syringe. The formulation we use contains 100 mg in 0.5 mL. We often have people start with a dose of 5-10 units (10-20 mg). We are not recommending a specific dosage for the readers of this document, however, we are including this information because we believe it is important to be aware that dosing needs to be very cautious, especially when new to NAD.
    - NAD can cause histamine reactions and has a variety of immunostimulating properties. As a result, some patients with chronic infections, such as severe chronic Lyme disease or mold toxicity, can be sensitive and have an aberrant reaction when they first take NAD.
    - There's a lot of talk about NAD in the popular press, and I just want to emphasize that although it may be beneficial, I would be very careful with it, and encourage you to only take it under the guidance of a qualified health practitioner, and be aware that some patients can have reactions to it.
    - We always recommend taking a TMG supplement with it to utilize methyl group donation to aid utilization and metabolism.

Exosome Therapy:

- This is a modality that is not widely available and is probably not going to be available in the short term.

- We have submitted an IND to the FDA - if that passes, we are hopeful to study the effects of exosomes in patients who have had exaggerated immune responses.

- Let us be very clear - this is an extremely nuanced situation for a doctor and a patient to manage. This is because, on the one hand, regenerative medicine tends to balance

immune reactions, but we don't want to do that to the detriment of reducing antibody response.

- I don't think that exosomes should be first, second, or even third-line therapy. That being said, I think it's important that it's studied, because it may have the ability to help benefit the very small percentage of patients who are having an extreme reaction to a vaccine.

Peptide Therapy:

- Peptide therapy is a relatively new field in medicine that uses cellular signaling molecules to help modulate biochemistry in the body.

- Peptides are made up of a sequence of amino acids. These sequences, if ingested by mouth, tend to be broken down in the stomach like other proteins, so most often they are injected with an insulin syringe.

- The most famous peptide is insulin - it's a "baby protein" that helps lower blood sugar by stimulating glucose channel openings. There are a variety of other peptides that can be used.

- Peptide therapy is relatively complex, and because it involves injecting oneself with medication in an aseptic manner, it should be done under the guidance of a qualified healthcare practitioner. This is even more important in the setting of complex illness or in the setting of pre- and post-vaccine use.

- Peptide therapy may not be available in some jurisdictions. So it is very important that you pay attention to the regulations in your country.

- In broad terms, there are several categories of therapeutic peptides that affect human physiology.
    - Immune modulating peptides - the most relevant being thymosin alpha-1. The second most relevant immune modulating peptide is thymosin beta-4. Both TA-1 and TB-4 have been somewhat controversial in the United States over the last year, and because of regulatory changes, compounding pharmacies are no longer supplying them to doctors. Thymosin beta-4 is contraindicated in the setting of cancer. There are some new immune modulating peptides on the horizon.
    - Antimicrobial peptides include LL-37.
    - Anti-inflammatory/tissue healing peptides - the most relevant of which is BPC-157. It also has some effects on blood vessels, and some patients have noted that it is beneficial for flu-like symptoms after the vaccine.
    - Mitochondrial supporting peptides - the most commonly available versions of these are MOTs-C, humanin, and FGL

    - Neuromodulating peptides - this document is primarily intended to support people before and after the vaccine. However, we have had both long-haul COVID patients and patients who have had the vaccine who have had some neurological consequences afterwards. The neurological peptides include Semax and Selank. Semax increases BDNF, which supports nerve function and growth. Selank modulates GABA and serotonin.
    - Growth-hormone secretagogues - I mention this category only because some patients with complex illness and immune problems, particularly patients with severe cases of mast cell activation syndrome and POTS/dysautonomia, are susceptible to flushing from growth hormone secretagogues.

- I cannot emphasize enough that there is a wide range of dosages with peptides and this is not the best place to start if you are new to the peptide conversation.

- At BioReset, we are co-founding an international peptide academy with the aim of educating practitioners and patients about how to use peptides. There will be academic and educational meetings in 2022, as well as weekly calls starting in the coming weeks. For information on any of these courses, please check out http://beta.internationalpeptideacademy.com

- **Thymosin alpha-1**
    - Thymosin alpha-1 is a peptide which has a variety of immunostimulating and immunomodulating effects
    - In general, we're not recommending that patients start taking thymosin alpha-1 before a vaccination. However, there are many patients who are taking this peptide and may wonder what to do about it when the time comes to get a vaccine. There is some preliminary research that supports TA-1's use as a vaccine adjuvant to other vaccines. There are also patients who have used it after a vaccine, with positive benefits in modulating inflammatory symptoms.
    - TA-1 is unavailable in the United States, however we have patients world-wide, so we are including content about this because we are having a global conversation.
    - TA-1 is an agonist of TLR-9 and TLR-2 on dendritic and myeloid cells, which stimulates the adaptive immune response (high dose Vitamin A also upregulates TLR receptors)
    - By increasing T-cell dependent antibody production, it has been suggested that it may enhance the immune response to vaccines
    - Increases the production of regulatory T cells, which inhibits cytokine production and dampens the immune response to prevent cytokine storm and autoimmunity

- **BPC-157**
    - Gastric peptide involved in regulating mucosal tissue repair, particularly in the GI tract
    - Modulates the inflammatory response and supports connective tissue repair

    - Has been shown in animal studies to prevent experimentally-induced anaphylactic reactions and therefore may be mast cell stabilizing

- **Thymosin beta-4**
    - Neuroprotective peptide involved in the process of neurologic development
    - Anti-inflammatory and anti-apoptotic, it promotes angiogenesis, tissue repair, stem cell differentiation, and cell migration

Additional Relevant Information:

I wanted to include a very brief description of some common immune sequelae we see in our clinic. A full explanation of their complex physiology is beyond the scope of this document, but we are referencing them so that you are aware of them, because patients who have had COVID-19 illness, long-haul COVID, or vaccine reactions may present with these symptoms.

- **Mast cell activation syndrome (MCAS)** is an immune disorder characterized by a hyper-active response of mast cells, a type of immune response involved in an allergy or anti-parasitic immune response. In the presence of triggering stimuli, mast cells release histamine and a host of other inflammatory mediators that can cause changes in heart rate, blood pressure, temperature regulation, flushing, itching or skin rashes, breathing changes, anxiety, insomnia, swelling, and diarrhea. In MCAS patients, these triggers can include stress, food ingredients, herbal or nutritional supplements, acute illness, antibiotic or other drug therapies, injections or other skin irritants, among others. This condition is difficult to treat because of its effect on quality of life and capacity to tolerate other medical therapies (natural or conventional). We tend to see this condition most commonly in the context of Lyme and other vector-borne infections, mold toxicity, toxicant-induced loss of tolerance (aka TILT, or multiple chemical sensitivity syndrome), and parasitic infection, but have also seen in in long-haul COVID patients.

- **Dysautonomia and Postural Orthostatic Tachycardia Syndrome (POTS)** are neurological disorders characterized by disruption to the normal function of the autonomic nervous system (ANS). The ANS, composed of both the sympathetic and parasympathetic nervous systems, regulate nearly all involuntary organ functions, including digestion, breathing, heart rate and blood pressure, peripheral blood vessel activity, sweating, and more. Dysregulation here can manifest as dramatic increases in heart rate while standing (POTS), inability to tolerate temperature changes, fluctuating blood pressure, fatigue or swelling after meals, or disruptions to digestion. Dysautonomia can be related to a host of other neurological disorders, but we see it commonly in the context of chronic immune disorders. MCAS and dysautonomia are closely related, as mast cells can degranulate in close proximity to autonomic nerves, affecting their function.

We hope you found this useful and look forward to a continued discussion.

In Health,
Matt Cook, MD
Harry McIlroy, MD
Muhammad Monsour, ND

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Addendum:
We are building a reference list that we will continue to update in the coming months with new information and data. We will begin to reference it throughout the document.