



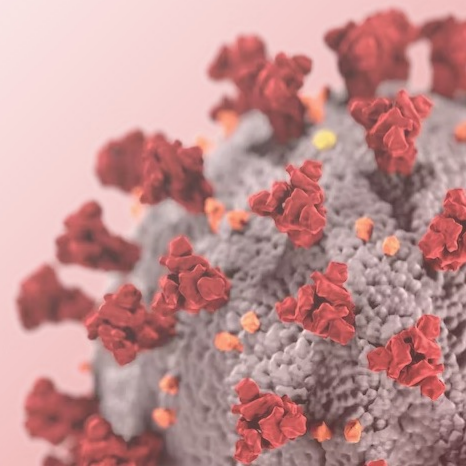
**EMERGING APPROACHES TO TREATING
SPIKE PROTEIN-INDUCED DISEASES**

April 28-29, 2023 • Fort Worth, Texas

Inflammation and Reactivated Infection Post Johnson and Johnson COVID-19 Vaccine

Presented By:

Keith Berkowitz, M.D.



COVID-19 Vaccine Information

COVID – 19 VACCINE INFORMATION from the CDC as of April 1, 2023

- 672 million doses of COVID-19 vaccines have been administered in the United States as of March 1, 2023
- During this time, VAERS has received 19,476 preliminary reports of death among individuals who received the COVID-19 vaccine
- CDC and FDA has identified nine deaths causally associated with the J&J/Janssen COVID-19 vaccination.

COVID-19 Vaccine Information

Johnson and Johnson's Janssen COVID 19 Vaccine

A vector vaccine:

- Uses genetic material from the COVID-19 virus is inserted into a different kind of weakened live virus, such as an adenovirus
- Weakened virus (viral vector) serves as the delivery system
- When the viral vector gets into the cells it delivers genetic material from the COVID-19 virus that gives the cells instructions to make copies of the S protein
- Once the cells display the S proteins on their surfaces, the immune system responds by creating antibodies and defensive white blood cells

Case Review: History

27-year-old male with a history of prior COVID- 19 infection and Lyme disease who “blacked out” one month after his Johnson and Johnson COVID-19 vaccine.

Other exhibited symptoms:

- Exercise intolerance
- Headaches
- Tachycardia
- Night sweats
- Vivid dreams
- Fatigue
- Gas and bloating



Risk of Injury Post Vaccination in Individuals with Previous COVID 19 Infection

Researchers in Canada conducted a prospective, multicenter, active surveillance cohort study between December 2020 and November 2021 to investigate the short-term safety of COVID-19 vaccination in adults previously infected with COVID-19.

- Total of 684,998 individuals who were vaccinated against COVID-19 infection were included in this analysis.
 - Within 1 week of receipt of the first vaccine dose, a higher percentage of previously infected individual experienced AEs capable of interfering with daily activities compared with those with no history of COVID-19 infection (range, 12%-16% vs 3%-12%, respectively).
 - The percentage of individuals who experienced severe AEs requiring emergency department admission or hospitalization following vaccination also was increased among those who were vs were not previously infected with COVID-19 (range, 0.6%-0.7% vs 0.2%-0.5%)

Bettinger JA, Irvine MA, Shulha HP, et al. [Adverse events following immunization with mRNA and viral vector vaccines in individuals with previous SARS-CoV-2 infection from the Canadian National Vaccine Safety Network](#). *Clin Infect Dis*. Published online October 31, 2022.



Case Review: Data

Timeline:

1. August 2020 – COVID Infection
 - a. Symptoms – lost of taste, smell, headaches and rapid heart rate
 - b. Treated with antibiotics and steroids
2. August 2021 – Positive IgM antibodies for Lyme Infection
 - a. Treated with 3 weeks of Doxycycline
3. September 7, 2021 – had J and J COVID-19 vaccine
4. October 11, 2021 - had an episode on “blacking out” and was taken to hospital
 - a. Found to have elevated inflammation markers:
 - C-reactive protein of 9.3 and erythrocyte sedimentation rate of 93
 - b. Found to have enlarged spleen and liver
 - c. Treated with steroids and intravenous antibiotics
 - d. Improvement only in heart rate and night sweats
5. August 22, 2022 – first clinic visit



Case Review: Data

First office visit – August 22, 2022

Vital signs:

	<u>Blood pressure</u>	<u>Pulse</u>
• Supine	120/70	97
• Sitting	120/74	105
• Standing	120/76	110

Physical exam:

Normal exam except for moderate abdominal bloating



Case Review: Lab Results

- White blood count is low at 3.8
- Hemoglobin is normal at 12.3
- Lyme titers - Positive IgM bands and negative IgG bands
- Negative titers for previous exposure to Epstein Barr virus
- Iron is low at 14
- Ferritin is elevated at 585
- Cortisol is high normal at 16.0
- C-reactive protein is elevated at 156.67
- D-dimer is normal
- MTHFR – one copy of 677 variant
- homocysteine level is normal

My Initial thoughts?

Lab work showed a low white blood count, elevated c-reactive protein and elevated ferritin level.

This was more like acute COVID-19 infection as opposed to COVID- 19 vaccine injury.



Case Review: Diagnoses

- Post – viral syndrome – secondary to vaccination
 - Epstein Barr virus titers were negative
 - Positive IgM bands consistent with acute Lyme disease
 - Reactivated COVID-19 infection
- Anemia
 - Low iron with elevated ferritin level
 - Most likely secondary to infection and inflammation
- Other potential issues
 - Gut microbiome disruption
 - Glucose/insulin dysregulation
 - Mitochondrial dysfunction
 - Fibrin clotting issue

Case Review: Treatment Protocol

Initial treatment Protocol

Post viral and Post inflammatory

- Ivermectin 0.1 mg/kg a day for 4 weeks
- Prednisone 15 mg a day for 7 days, 10 mg a day for 7 days and 5 mg a day for 7 days

Anemia

- Vitamin C supplementation
- Iron supplementation

Gut microbiome support

- Probiotic
- Colostrum



Case Review: Treatment Protocol

Dietary Changes

- Controlled carbohydrate diet
- Intermittent Fasting
 - Smaller and more easily digestible dinner
 - Finish eating by 6 pm

Lifestyle changes

- Light exercise only
 - No cardio
 - Walking or resistance training
- Sleep
 - 7 to 8 hours a night



Case Review: Follow -up

Follow-up at 6 weeks

- Mild improvement in symptoms:
 - Slight increase in energy
 - Decrease in heart rate
 - Still with exercise intolerance

Labs:

- Repeat labs did not show a decrease in CRP and still with one IgM band on western blot for Lyme disease.



Case Review: Protocol Adjustment

Increased emphasis on immunomodulation and mitochondrial support:

- Added low dose naltrexone started on 0.5 mg- goal is to increase dose to 4.5 mg a day.
- Arginine-Citrulline 500 mg one tablet 2 x day
 - Would avoid if individual has reactivated and/or acute Epstein Barr virus.
- Ubiquinol (Coq10) 200 mg once a day.

Case Review: Return

Follow up: March 2023

- Improved exercise tolerance
 - Now rides bicycle 3 mile a day
 - Able to walk on treadmill at a 4 mile per hour rate
 - Able to resume weight training
- Only 2 headaches in the last 6 weeks
- Resumed full work schedule including travel
- Now 75 to 80% better

Will continue current treatment as well as increase low dose naltrexone to the full therapeutic dose of 4.5 mg.



Case Review: Repeat Labs

Repeat labs, March 2023

- White blood count is 4.2 (improved from 3.8)
- Hemoglobin is 12.5 (was 12.3)
- Lyme titers – One positive IgM bands and negative IgG bands
- Iron is 23 (was 14)
- Ferritin is 378 (was 585)
- Cortisol is 12.8 (was 16.0)
- C- reactive protein is 97.67 (was 156.67)
- Insulin is 21.8 (was not measured at first visit)

Treating the Vaccine- Injured Patient

Suspected mechanisms of injury in this patient:

1. Post – viral
2. Post – inflammatory
3. Methylation Issues
4. Mitochondrial Dysfunction
5. Blood Glucose Disruption
6. Gut Microbiome Disruption



Treatment: Ivermectin

Mechanism of action as an anti-viral and as an anti-inflammatory

- Demonstrates IMP α/β -dependent nuclear transfer inhibition and reduced virus replication
- Binds to the viral N phosphoprotein and M protein is suggestive of its role in inhibiting viral replication and assembly
- Promotes the expression of several Interferon-related genes
- Blockades the activation of NF-kB pathway and inhibition of TLR4 signaling
- Inhibits STAT-3 through direct inhibition which is responsible for upregulation of proinflammatory cytokines, TNF α , and IL-6 in macrophages

Zaidi, Asiya and Dehgnai-Mobaraki: The mechanisms of action of ivermectin against SARS-CoV-2—an extensive review.

The Journal of Antibiotics volume 75, pages 60–71 (2022)



Treatment: Low Dose Naltrexone

Mechanism of Action:

- Action on opioid receptors to increase release of β -endorphins
- Ability to reduce pro-inflammatory cytokines and increase anti-inflammatory cytokines
 - Blocks toll-like receptor signaling which decreases glial cell activation, decreases cytokines, decreases neuroinflammation
- Regulation of the opioid growth factor (OGF)/opioid growth factor receptors (OGFr) axis.
- Modulates T and B lymphocyte production

Toljan, Karlo, and Vrooman, Bruce., Low-dose Naltrexone, Review of Therapeutic Utilization, Med. Sci (Basel). Dec 6(4): 82, 2018.



Low Dose Naltrexone

Works to balance the TH1 and TH2 immune response:

- Th1-type cytokines tend to produce the proinflammatory responses responsible for killing intracellular parasites and for perpetuating autoimmune responses.
 - Interferon gamma is the main Th1 cytokine.
 - Excessive proinflammatory responses can lead to uncontrolled tissue damage, so there needs to be a mechanism to counteract this.
- The Th2-type cytokines include:
 - Interleukins 4, 5, and 13, which are associated with the promotion of IgE and eosinophilic responses in atopy
 - Interleukin-10, which has more of an anti-inflammatory response.
 - In excess, Th2 responses will counteract the Th1 mediated microbicidal action.

Berger, Abi., Th1 and Th2 responses: what are they? BMJ. 2000 Aug 12; 321(7258): 424.



Treatment: A Clinician's Perspective

- “Start low and go slow” – begin at a dose of 0.5 to 1.5 mg a day and increase (0.5 to 1.5 mg) every 2 weeks to a maximum dose of 4.5 mg
 - Not everyone needs to be increased to dose of 4.5 mg to benefit
- Have patience – some patients may not see benefit for 3 to 6 months
- Some individuals do not tolerate medication because of insomnia
 - Change dosing from evening to morning
- Length of treatment can be 3 -12 months
 - Individuals with autoimmune disease may need to stay on medication for a longer duration

Methylation: MTHFR Gene

According to the American Heart Association, 30 to 40 percent of the American population may have a mutation at gene position C677T; and this gene prevents the body from converting folate into methylfolate.

- This can increase homocysteine levels
 - Increase risk of arterial damage and blood clots in your blood vessels.
- L-methylfolate functions in the brain as the building block for producing mood neurotransmitters like serotonin, norepinephrine, and dopamine.
 - Increases risk for depression and anxiety
- Impairs nitric oxide synthesis and decreased the ability to produce glutathione

Balnis, Joseph, et. al. **Blood DNA methylation and COVID-19 outcomes**, *Clinical Epigenetics* volume 13, Article number: 118 (2021)



Blood Glucose Disruption

Infection with SARS-COV19 impacts the expression of insulin/IGF signaling pathways in liver, lung, adipose tissue and pancreatic cells.

- This can lead to a mismatch in glucose and insulin levels:
 - High glucose levels with inappropriately low insulin production.
 - Seen in several of my type II diabetes mellitus patients.
 - Many never required medication previously.
 - Low glucose levels with inappropriately elevated insulin production.
 - Often seen in “thin” women.
 - Can be seen together with hormone imbalance.
 - Low progesterone with high testosterone and high total estrogen levels.

Shin, J., *et al.* (2022) SARS-CoV-2 infection impairs the insulin/IGF signaling pathway in the lung, liver, adipose tissue, and pancreatic cells via

IRF1. *Metabolism*. doi.org/10.1016/j.metabol.2022.155236.



Mitochondrial Dysfunction

The mitochondria's main role is to generate ATP by using the energy released during the oxidization of the food we consume:

- ATP is the primary energy source for most biochemical and physiological processes, such as growth, movement and homeostasis.
- A major produce of reactive oxygen species which makes them very susceptible to damage by oxidative stress.
 - Oxidative stress is a condition of increased amounts of reactive oxygen/nitrogen species.
 - Oxidative stress results from an imbalance between free radicals and antioxidants.

Note: This can be a contributing factor in mitochondrial dysfunction, inflammatory pathways, and brain dysfunction.

Wood E, Hall KH, Tate W. Role of mitochondria, oxidative stress and the response to antioxidants in myalgia encephalomyelitis/chronic fatigue syndrome: a possible approach to SARS-CoV-2 'long-haulers'? *Chronic Dis Transl Med.* 2021;7(1):14-26.



Mitochondrial Dysfunction: Treatment Options

Coenzyme Q10:

- Only lipid-soluble antioxidant that is synthesized in humans
- Reduces reactive oxidative species
- Mostly found in the mitochondrial membrane with highest concentrations in the metabolic tissues including the heart, liver and muscle
- Proposed mechanism of action is that CoQ10 decreases the impact of pro-inflammatory cytokines and restores the function of exhausted T cells
 - This seems to happen in individuals with “long haul” or chronic infective/inflammatory conditions

Wood E, Hall KH, Tate W. Role of mitochondria, oxidative stress and the response to antioxidants in myalgic encephalomyelitis/chronic fatigue syndrome: a possible approach to SARS-CoV-2 ‘long-haulers’? *Chronic Dis Transl Med.* 2021;7(1):14-26.



Gut Microbiome Issues

- The diversity of the actinobacteria phylum in the gut microbiota is decreased during COVID-19 infection.
- Bifidobacterium & Lactobacillus bacterium levels are decreased during a COVID-19 infection.
 - ***Bifidobacterium*** (Actinobacteria) → Immune-modulating effects that can help reduce cytokine storm, very important in our innate immune response.
 - ***Lactobacillus bacterium*** (Firmicutes) → major component of digestive tract and assists in immune response.
- Bacteroides and Enterobacteriaceae levels are increased during COVID-19 infection.



Gut Microbiome Issues

After BNT-162b2 COVID 19 vaccine changes in gut microbiome:

- Increased levels of gut bacteria including:
 - Bacteroides caccae
 - Alistipes shahi
- Decreased levels of gut bacteria including:
 - Adlercreutzia equolifaciens
 - Asaccharobacter celatus
 - Blautia obeum
 - Blautia wexlera
 - Dorea formicigenerans
 - Dorea longicatena
 - Coprococcus comes
 - Streptococcus vestibularis
 - Collinsella aerofaciens
 - Ruminococcus obeum

Overall, a substantial decrease in gut microbiome biodiversity.

Leung, John, Interaction between gut microbiota and COVID-19 and its vaccines; World J Gastroenterol. 2022 Oct 28; 28(40): 5801–5806.



Treatment: Colostrum/Bovine Immunoglobulin

Enhances immune response:

- Contains a high concentration of lactoferrin and immunoglobulins.
- Contains cytokines and proline-rich polypeptides (which encourages growth of white blood cells and reduces excessive oxidative stress).
- Significantly reduced NK cell and monocyte activities and lymphoproliferative responses to lipopolysaccharide stimulation.
 - Leads to anti-inflammatory activity.

Xu, Mei Ling, et al. **Effect of dietary bovine colostrum on the responses of immune cells to stimulation with bacterial lipopolysaccharide**; Arch Pharm Res 2014 Apr;37(4): 494-500.



Treatment: Lifestyle and Dietary Options

- ✓ Low carbohydrate Diet
- ✓ Low histamine Diet
- ✓ Intermittent Fasting: Autophagy
- ✓ Better sleep – restoration of circadian rhythm
- ✓ Infrared Sauna
- ✓ Resistance Training



Keith Berkowitz, MD, MBA

Center for Balanced Health

info@centerforbalancedhealth.com

212-459-1700

