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A Novel Approach to Treating COVID-19 Using Nutritional and Oxidative Therapies

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Abstract

Objective: This report is a case series of consecutive patients diagnosed with **COVID-19** treated with a nutritional and oxidative medical approach. We describe the treatment program and report the response of the 107 **COVID-19** patients.

Study Design: Observational case series consecutive.

Setting: A family practice office in a suburb of Detroit, Michigan.

Patients: All patients seen in the office from February through May 2020 diagnosed with **COVID-19** were included in the study. **COVID-19** was either diagnosed via PCR or antibody testing as well as those not tested diagnosed via symptomology.

Interventions: Oral Vitamins A, C, D, and iodine were given to 107 subjects (99%). Intravenous solutions of hydrogen peroxide and Vitamin C were given to 32 (30%) and 37 (35%) subjects. Thirty-seven (35%) of the cohort was treated with intramuscular ozone. A dilute, nebulized hydrogen peroxide/saline mixture, with Lugol's iodine, was used by 91 (85%).

Main Outcome Measures: History and physical exam were reviewed for **COVID-19** symptoms including cough, fever, shortness of breath, and gastrointestinal complaints. Laboratory reports were examined for **SARS-CoV-2** results. Symptomatic improvement after treatment was reported for each patient consisting of *first improvement*, *mostly better*, and *completely better*.

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Keywords

SARS-CoV-2, COVID-19, ozone therapy, hydrogen peroxide therapy, Vitamin A, iodine, Vitamin C, Vitamin D, immune system, antiviral.

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Abstract (Continued from page 1)

Results: There were a total of 107 patients diagnosed with **COVID-19**. Thirty-four were tested for SARS-CoV-2(32%) and twenty-seven (25%) tested positive. Three were hospitalized (3%) with two of the three hospitalized before instituting treatment and only one requiring hospitalization after beginning treatment. There were no deaths. The most common symptoms in the cohort were fever (81%), shortness of breath (68%), URI which included cough (69%), and gastrointestinal distress symptoms (27%). For the entire cohort, first improvement was noted in 2.4 days. The cohort reported symptoms mostly better after 4.4 days and completely better 6.9 days after starting the program. For the **SARS-CoV-2** test positive patients, fever was present in 25 (93%), shortness of breath in 20 (74%) and upper respiratory symptoms including cough in 21 (78%) while gastrointestinal symptoms were present in 9 (33%). The time to improvement in the **SARS-CoV-2** test positive group was slightly longer than the entire cohort.

Conclusion: At present, there is no published cure, treatment, or preventive for **COVID-19** except for a recent report on dexamethasone for seriously ill patients. A novel treatment program combining nutritional and oxidative therapies was shown to successfully treat the signs and symptoms of 100% of 107 patients diagnosed with **COVID-19**. Each patient was treated with an individualized plan consisting of a combination of oral, IV, IM, and nebulized nutritional and oxidative therapies which resulted in zero deaths and recovery from **COVID-19**. Keywords: **SARS-CoV-2**, COVID-19, ozone therapy, hydrogen peroxie therapy, Vitamin A, iodine, Vitamin C, Vitamin D, immune system, antiviral.

1. Introduction

SARS-CoV-2 is the strain of coronavirus that causes coronavirus disease 2019 known as **COVID-19**. To date, **COVID-19** has infected 7,669,872 cases worldwide and 2,090,553 cases in the US with 116,347 reported fatalities (as of 6.13.2020).[1] **COVID-19** is a pandemic that is unparalleled in the modern world and the global response to **SARS-CoV-2** has no parallel in history. Coronaviruses are found in many bat and bird species, which are believed to be natural hosts.[2] It is estimated that coronaviruses have been around from 10,000 to millions of years. Coronaviruses are pathogenic viruses native to birds and mammals. They are classified into four subspecies: alpha-, beta-, gamma-, and delta- coronavirus.[3] Alpha- and beta- coronaviruses are found exclusively in mammals and gamma- and delta-coronavirus primarily infect birds.[4] Coronaviruses include a family of viruses that contain an RNA genome. Some of these viruses have been shown to cause illness in animals and humans.

SARS (severe acute respiratory syndrome) was discovered in 2003.[5] It was described as an outbreak of atypical pneumonia in Guangdong Province, Peoples Republic of China. SARS, which occurred during 2002-2003 infected approximately 8,098 and resulted in 774 deaths. The outbreak was primarily concentrated in Southeast Asia and Toronto, Canada although the outbreak spread to more than 24 countries. SARS was found to be caused by a strain of coronavirus that infects the epithelial lining within the lungs.[6] Prior to the SARS outbreak, coronaviruses were only thought to cause mild influenza-like illnesses in humans.

The second major human outbreak of coronavirus was in 2012 in Saudi Arabia. It was referred to as MERS (Middle East Respiratory Syndrome). It spread to several countries including the US. Most people infected with MERS suffered with respiratory problems including cough and shortness of breath. The World Health Organization confirmed 2,519 cases of MERS as of January, 2020.[7]

SARS-CoV-2 is a new strain of coronavirus that has not been known to previously infect humans. **COVID-19** was first identified in Wuhan, China in December 2019. China informed the WHO that a novel strain of coronavirus was causing severe illness. It was named **SARS-CoV-2** as the cause of **COVID-19**. The virus was sequenced and found to most resemble viruses found in bats and pangolins.[8] **SARS-CoV-2** was found to be highly transmissible between humans. **SARS-CoV-2** can be diagnosed via nasal swab PCR testing. According the Centers for Disease Control and Prevention, people with **COVID-19** have a wide range of symptoms reported from mild symptoms to severe illness.[9] People with these symptoms may have **COVID-19**:

- Cough
- Shortness of Breath or difficulty breathing

Or at least two of these symptoms:

- Fever
- Chills
- Repeated shaking with chills
- Muscle pain
- Headache
- Sore throat
- New loss of taste or smell

The CDC further states, that this list is not inclusive. According the CDC, the signs and symptoms of **COVID-19** present at illness vary, but over the course of the disease, most persons with **COVID-19** will experience the following:[10]

- Fever (83-99%)
- Cough (59-82%)
- Shortness of breath (31-40%)
- Sputum production (28-33%)

Our patients' symptomology correlated well with the percentages reported by the CDC.

We will present data on clinical presentation and treatment provided to help patients recover from **COVID-19** symptoms. This treatment program has been utilized for over 20 years (with some variations) in treating patients suffering from viral illnesses such as influenza-like disease. This treatment program was not designed to cure a viral illness rather its purpose is to provide a therapeutic regimen designed to support the immune system when it is challenged with a viral infection.

2. Methods

The setting for this retrospective review is an outpatient medical office (referred to as CHM) consisting of five practitioners. The office is in the metropolitan Detroit area, which was one of the hot spots for **COVID-19**. The practitioners include three medical doctors as well as a nurse practitioner and a physician's assistant. For the calendar year of 2020, charts were retrospectively reviewed for the presence of **COVID-19** diagnosis occurring from February 2020 through May 2020. The charts were analyzed for clinical symptoms, physical findings, imaging and coronavirus testing results. Additionally, the charts were analyzed for interventions provided and duration to relief of symptoms. Three endpoints were taken from the charts – hospitalization, death, and time to improvement.

All patients gave fully informed consent for integrative medical management of their condition. Historical information from the charts included age, sex, birthdate, initial date of service, care provider, past medical history, medications, and nutritional supplements. The number of days of illness prior to being seen by a provider was documented as well.

For x-ray imaging we used the report provided by the radiologist. Coronavirus testing was done through outpatient and inpatient laboratories. Coronavirus was diagnosed by PCR nasal swab testing.

The interventions provided at the outpatient medical office included oral supplementation of iodine, Vitamins A, C and D, intravenous hydrogen peroxide and Vitamin C, intramuscular ozone injections, and a nebulized solution of dilute hydrogen peroxide and iodine.

Oral dosing consisted of taking the following supplements for four days at the first sign of symptoms or at the direction of the practitioner. The supplements consisted of:

- Vitamin A: 100,000 IU/day*** in the form of emulsified Vitamin A palmitate
- Vitamin C: 1,000 mg/hour while awake in the form of ascorbic acid until bowel tolerance (loose stools) was reached
- Vitamin D3: 50,000 IU/day in an emulsified form
- Iodine: 25 mg/day in the form of Lugol's solution or tableted Lugol's solution

Most patients were instructed to nebulize a dilute solution of 0.04% hydrogen peroxide in normal saline. The solution was mixed for the patient in the office. A sterile 250 cc bag of normal saline was injected with 3 cc of 3% food grade hydrogen peroxide and 1 cc of magnesium sulfate. The patient was instructed to draw off 3 cc of the dilute solution and nebulize it hourly until symptoms improve. Additionally, the patient was instructed to add in one drop of 5% Lugol's solution to the dilute hydrogen peroxide mixture. As the symptoms improved, the frequency of nebulizing could be reduced by the patient.

If symptoms worsened or there was a concern that the patient was suffering from a more severe case, the patient was advised to come to the office and receive intravenous injections of Vitamin C and hydrogen peroxide along with intramuscular injections of ozone. The dosing of these items is shown below:

- Vitamin C: 2.5 grams of sodium ascorbate (5 cc of a 500 mg/cc ascorbic acid solution) mixed with an equal amount of sterile water given as an intravenous push over 2-3 minutes.

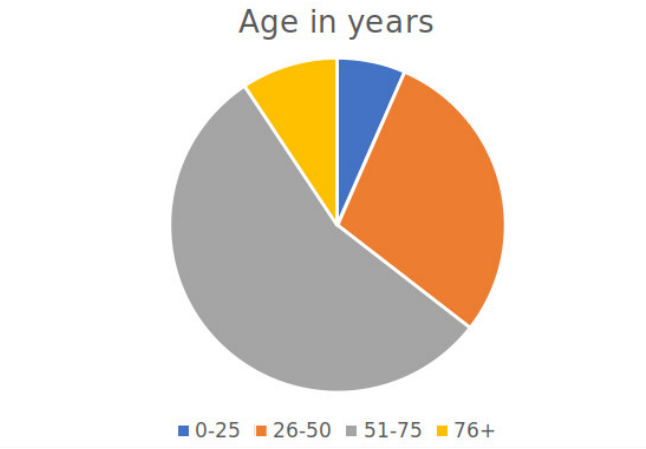

Figure 1. Patient Age distribution

- Hydrogen peroxide: 30 cc of a 0.03% solution of dilute hydrogen peroxide given as an intravenous push over 2-3 minutes
- Ozone: 20 cc of 18 mcg/cc ozone (as an oxygen/ozone gas mixture) given in each buttock as an intramuscular injection

3. Results

There were 107 patients identified in our chart review among five practitioners. **Table I** outlines the patient characteristics of the sample. The age of patients ranges from 2-85 years old with an average age of 54.2 and median age of 56.5. 80 patients were female (75%) and 27 were male (25%). The major comorbid conditions of the sample include hypothyroidism (18%), hypertension (10%), asthma (8%), Lyme disease (6%), Hashimoto's disease (5%), cigarette smoking (3%), Grave's disease (2%), chronic sinusitis (2%), diabetes (2%) and cancer (2%).

Figure 1 exemplifies the age distribution of the 107-patient population at the practice. The majority of the patients were between 51-75 years old (59%). The second highest cohort was between 26-50 years old (31%). Followed by those 76 years old and older (10%) and those aged 2-25 (7%).

Table II illustrates the patient symptoms of the total cohort. The most common patient symptom was fever (81%), shortness of breath (68%), URI (69%) and GI symptoms (27%).

Table 1. Patient Characteristics

	N(%)
Total patients	107(100)
Age	
Range	2-85
Average	54.2
Median	56.5
Sex	
Male	27 (25)
Female	80 (75)
Comorbid Conditions	
Hypothyroidism	19 (18)
Hypertension	11 (10)
Asthma	9 (8)
Lyme Disease	6 (6)
Hashimoto's disease	5 (5)
Smokers	3 (3)
Grave's disease	2 (2)
Chronic sinusitis	2 (2)
Diabetes	2 (2)
Cancer	2 (2)

Table 2. Patient Symptoms 'Total Cohort'

	N (%)
Fever	87 (81)
Shortness of breath	73 (68)
URI (symptoms including cough)	74 (69)
GI (diarrhea, loose stools, pain)	29 (27)
Total patients	107 (100)**

Table 3 demonstrates the interventions that the patients received from CHM (total cohort). The most common intervention was a protocol of oral supplements, including Vitamin A, Vitamin D, Vitamin C, and iodine. 106 patients of the 107 total patients were taking oral supplements (99%). The other interventions at CHM include 32 patients receiving IV hydrogen peroxide (30%), 37 patients receiving IV Vitamin C (35%), 37 patients receiving intramuscular ozone injections (35%), 91 patients receiving a nebulized solution of normal saline and dilute hydrogen peroxide (85%), and 91 patients receiving nebulized iodine (85%).

Figure 2 shows the average number of days that patient reported symptomatic improvement after CHM interventions (for total cohort). On average, patients reported their first improvement by 2.4 days following CHM interventions. Patients reported feeling mostly better by 4.4 days following interventions. Patients reported feeling completely better after 6.9 days following CHM interventions.

Table 4 illustrates the disease course in the total cohort. 34 of the 107 total patients (32%) were tested for COVID-19. Of those 34 tested, 27 patients tested positive for COVID-19 (79%). Therefore, 25% of the entire cohort (107 patients) had tested positive for COVID-19.[1] Of the total 107 patients, 0 died (0%).

Table 5 illustrates the symptoms of the COVID-19 cohort which was similar to **Table 2** for the entire cohort.[2] **Figure 3** shows the symptomatic improvement after intervention in the **SARS-CoV-2** laboratory positive cohort. Compared to the entire cohort (**Figure 2**), there was approximately a one day longer time period to feeling *mostly better* and *completely better* for those who tested positive for **SARS-CoV-2** as reported by the patients.

Table 3. Patient Interventions

INTERVENTION	total (cohort) **N (%)**
Total patients	107 (100)**
Oral supplements	106 (99)
IV H202	32 (30)
IV Vitamin C	37 (35)
IM Ozone	37 (35)
Nebulized NS/H202	91 (85)
Nebulized Iodine	91 (85)

Table 4. Disease Course

	N (%)
Total cohort	107 (100)
Tested for COVID-19	34 (32)
Tested positive for COVID-19	27 (25)
Hospitalized	3 (3) *
Death	0 (0)

* Of the three patients hospitalized, two were hospitalized before instituting treatment One was hospitalized on the oral Vitamin regimen of Vitamins A, C, D, and iodine. All three made a full recovery and were treated with nebulized hydrogen peroxide and iodine.

Table 5. Symptoms of COVID-19 Positive Cohort

	N (%)
COVID positive patients	27 (100)**
Fever	25 (93)
Shortness of breath	20 (74)
URI (includes cough)	21 (78)
GI	9 (33)

**Two patients in the SARS-CoV-2 positive cohort reported a return of mild symptoms after reporting a resolution of major symptoms. One patient reported feeling foggy in his head and another reported a fast heart (90-100 bpm) along with mild shortness of breath with any mild exertional activity. A workup on both failed to find a cause for the symptoms.

[1] Of the 107 total patients, three were hospitalized (3%) with two of the three hospitalized before beginning treatment.

[2] Two patients in the SARS-CoV-2 positive cohort reported a return of mild symptoms after reporting a resolution of major symptoms. One patient reported feeling foggy in his head and another reported a fast heart (90-100 bpm) along with mild shortness of breath with any mild exertional activity. A workup onboth failed to find a cause for the symptoms.

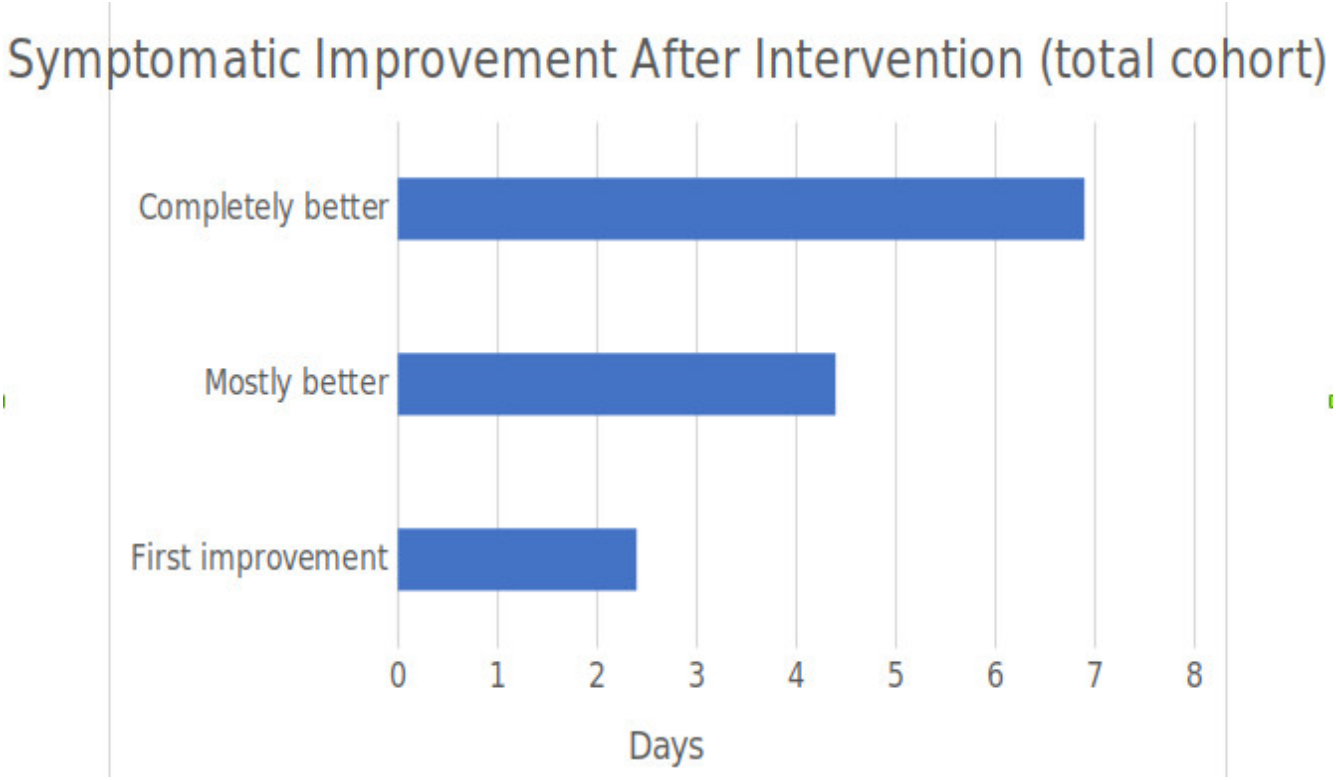

Figure 2. Intervention Results

4. Discussion

COVID-19 is a worldwide pandemic caused by coronavirus. Currently, there is no vaccine or cure for **COVID-19**. Dexamethasone has been reported to reduce hospitalized case mortality.[11] Those who have recovered from **COVID-19** have done so because their immune system was successful in fighting off the illness. Therefore, a successful treatment for **COVID-19** will have to either have viricidal activity or work by aiding the immune system's response in fighting the pathogen. Many feel **COVID-19** will come back during the next flu season—fall/winter of 2020-2021. Therefore, there is an urgent need for any therapy that supports the host's immune system and allows for an uneventful recovery from the illness.

This cohort study consisted of a retrospective review of 107 patients who were either diagnosed as **COVID-19** positive by PCR nasal swab testing or presumed to have **COVID-19** due to symptomatology. The most common symptom in our cohort was fever. The fever was reported as fluctuating varying between 99-102 degrees Fahrenheit for most subjects. The next most common symptom included upper respiratory symptoms which included a rhinorrhea, drippy eyes, cough, and congestion. Shortness of breath was the third most common complaint. Gastrointestinal distress, though common, was lower on the symptom list. Although symptoms varied between patients, all patients exhibited symptoms that could be consistent with a viral pathology.

Treatments of the cohort consisted of first using oral nutrient therapies. The vast majority—91 (88%) started taking vitamins A, C, D3 and iodine at the first sign of a viral illness such as a cough, runny nose, sore throat, etc., All subjects (100%) took vitamin C in suggested doses of at least 3-5,000 mg/day of ascorbic acid. Three patients took vitamins C and D only.

There were three hospitalizations in the cohort group. One patient was taking the oral protocol of vitamins A, C, D and iodine when he became ill with a cough and fever. His condition worsened over the next seven days and was admitted to the hospital where he was diagnosed with pneumonia. He was treated with antibiotics. He phoned the

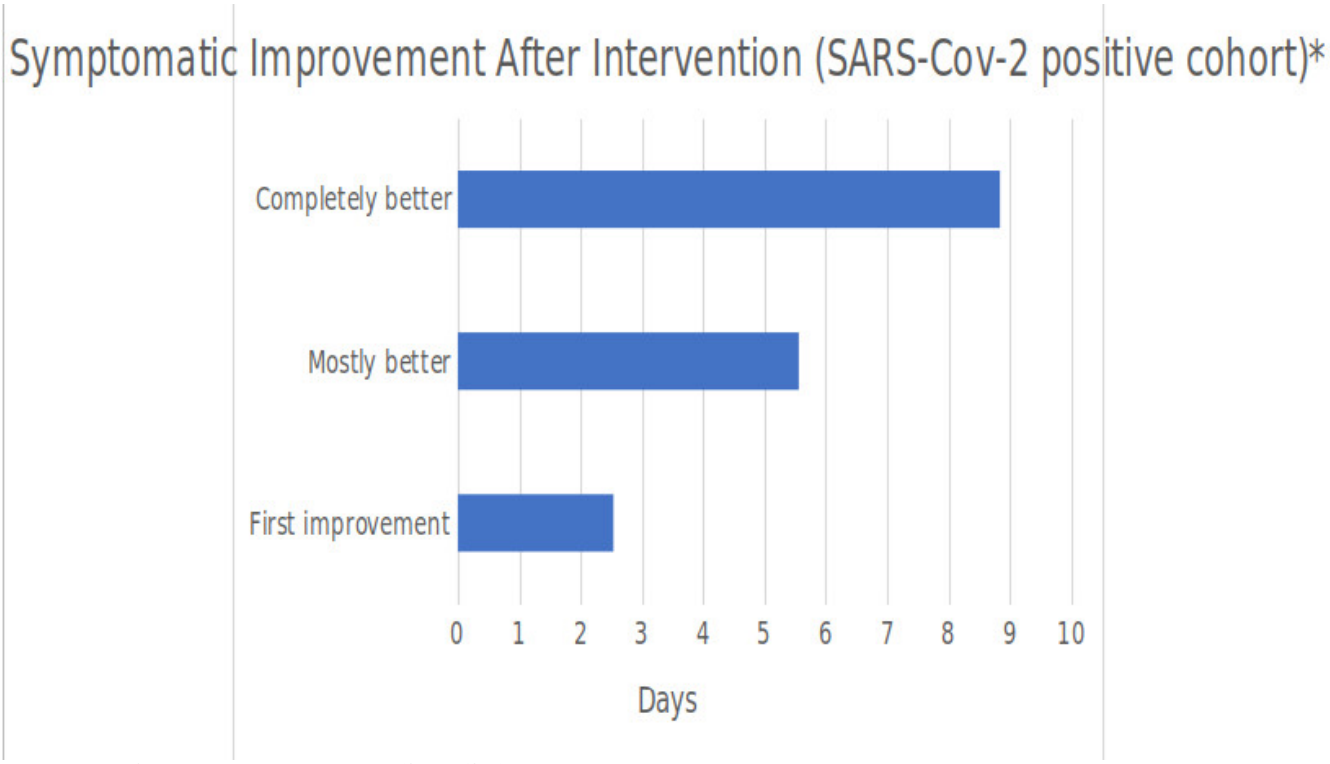

Figure 3. *Two patients in the **SARS-CoV-2** positive cohort reported a return of mild symptoms after reporting a resolution of major symptoms. One patient reported feeling foggy in his head and another reported a fast heart (90-100 bpm) along with mild shortness of breath with any mild exertional activity. A workup on both failed to find a cause for the symptoms.

office after he was discharged from the hospital because he was having breathing difficulties. He started nebulizing hydrogen peroxide and felt an immediate improvement in his breathing difficulties from this therapy. By the third nebulized therapy he reported to being 80% improved. He stated his breathing difficulties began to return to normal after day two of nebulizing every 2 hours while awake. The other two patients started our protocol after being hospitalized for **COVID-19**. One of the two was recently diagnosed with acute myelogenous leukemia and recently received chemotherapy. Both were discharged still symptomatic with breathing difficulties and a severe cough. Both patients were treated with nebulized hydrogen peroxide and iodine as well as the oral protocol of vitamins A, C, D, and iodine. All three patients fully recovered.

4.1 Vitamin A

Vitamin A consists of a group of retinoid compounds that have a wide range of physiological effects including the support of immune system functioning. Vitamin A deficiency is a worldwide problem affecting 250 million preschool children and half of all countries.[12] In children, vitamin A supplementation has been shown to dramatically decrease the mortality from the viral illnesses such as measles and diarrheal infections.[13]

Over 100 years ago, — before the chemical structure was elucidated — studies of vitamin A pointed to its important role in immune system functioning. Fat in butter, a good source of vitamin A, improved the outcome of infections in malnourished animals and humans.[14] Rats were shown to be more susceptible to infections when they were vitamin A deficient.[15] Vitamin A is fundamental in maintaining the integrity of the epithelium.[16] Vitamin A deficiency has been associated with dis-

ruptions in normal epithelium of the respiratory tract[17][18] and gastrointestinal tissue.[19][20] Vitamin A has been shown to be an important regulator of monocyte differentiation and function.[21]

COVID-19 is characterized by cytokine storm in the severely ill.[22] Therapies that lower cytokine formation are being investigated. Retinoic acid, when added to monocytic, myelomonocytic, or dendritic cell line cultures promotes cellular differentiation and influences the secretion of key cytokines produced by macrophages including TNF-α, IL-1β, Il-6, and IL-12. It has been hypothesized that supplementation with preformed vitamin A may down-regulate the secretion of specific proinflammatory cytokines such as TNF- α and Il-6 by macrophages.[23]

Acute respiratory distress syndrome (ARDS) accompanied by respiratory failure is a major cause of death from **COVID-19**.[24][25] Treatments to combat respiratory failure are urgently needed.

In vitro and *in vivo* studies have found that IgA antibodies can neutralize intracellular pathogens including viruses by inhibiting or blocking their attachment to epithelial cells.[26][27][28] Researchers studying the acute humoral response to **SARS-CoV-2** in serum and bronchoalveolar fluid of 145 patients with **COVID-19** reported that early **SARS-CoV-2** specific humoral responses were found to be typically dominated by antibodies of the IgA isotype.[29] Furthermore, the subjects who had the highest levels of IgA against the spike protein for **SARS-CoV-2** were the ones who had the greatest ability to neutralize the virus. Vitamin A deficiency has been shown to inhibit the production of influenza-specific IgA in mice.[30] Furthermore, vitamin A supplementation has been shown to increase IgA levels.[31]

4.2 Vitamin C (Ascorbate)

A Chinese report of intravenous vitamin C (IVC) infusion for 50 moderate to severe **COVID-19** subjects found all patients eventually recovered and discharged from the hospital. The subjects were given between 10 and 20 g of IVC per day over a period of 8-10 hours.[32] In 2017, Paul Marik, M.D. developed a protocol for treating septic patients with IV vitamin C, thiamine, and hydrocortisone. The early use of vitamin C along with thiamine and hydrocortisone were found to be effective at preventing progressive organ dysfunction including kidney injury and in reducing mortality of patients with severe sepsis and septic shock. In CITRIS-ALI researchers reported a trial where ARDS patients were randomized to receive IV ascorbic acid or placebo every six hours for 4 days. Patients had to develop ARDS within 24 hours of I CU admission. The authors reported a reduction in 28-day all-cause mortality rate in those receiving IV vitamin C: 29.8% mortality in the treatment group versus 46.3% mortality in the placebo group.[33] **COVID-19** patients are characterized by elevated levels of inflammatory markers and oxidative stress such as hsCRP.[34] Vitamin C is known to have anti-oxidant and anti-inflammatory effects. Erythrocytes (red blood cells) can deliver oxygen to bodily tissues because they carry iron-containing hemoglobin which reversibly binds oxygen. Oxidative damage to red blood cells can impair the ability to deliver oxygen to tissues.[35] The management (and possibly the prevention of) oxidative stress in **COVID-19** may be addressed with the use of anti-oxidant therapies. High-dose IV vitamin C was found to have an antioxidant effect for lung epithelial cells.[36] Vitamin C has also been shown to prevent the oxidation of iron from its reduced ferrous state to the oxidized ferric form.[37] Intravenous (but not oral) ascorbate has been shown to act as a pro-drug for hydrogen peroxide creation in interstitial fluids in animal studies (see hydrogen peroxide discussion below).[38]

4.3 Vitamin D

Vitamin D is being researched as an effective treatment option for **COVID-19** patients. Researchers used 25-hydroxyVitamin D [25(OH)D] levels as a marker to predict clinical outcomes of **COVID-19** subjects.[39] Of 212 cases of **COVID-19**, serum 25(OH)D level was lowest in critical cases but highest in mild cases. The authors reported vitamin D is significantly associated with clinical outcomes. A logistic regression analysis reported that for each standard deviation increase in serum 25(OH)D, the

odds of having a mild clinical outcome rather than a severe outcome were approximately 7.94 times (OR=0.126, $p<0.001$) while interestingly, the odds of having a mild clinical outcome rather than a critical outcome were approximately 19.61 times (OR=0.051, $p<0.001$). The results suggest that an increase in serum 25(OH)D level in the body could either improve clinical outcomes or mitigate worst (severe to critical) outcomes, while a decrease in serum **25(OH)D** level in the body could worsen clinical outcomes of **COVID-2019** patients.

There are several mechanisms by which vitamin D could reduce the risk of influenza-like infections and death. Viral infections have been shown to disrupt airway epithelial cell junctions.[40] Vitamin D has been shown to maintain tight epithelial junctions and adherens junctions.[41]

Vitamin D has been shown to modulate cellular immunity and reduce cytokine storm by reducing the production of proinflammatory cytokines including TNF-α and interferon-γ as well as increasing the anti-inflammatory cytokines produced by macrophages.[42] A study comparing deceased rates for patients with **COVID-19** from countries with a large number of confirmed patients (including Germany, S. Korea, China, Switzerland, Iran, UK, US, France, Spain, and Italy) found a risk of severe **COVID-19** cases among patients with very low vitamin D levels is 17.3%, while the equivalent figure for patients with normal vitamin D levels is 14.6%–a reduction of 15.6%.

The authors hypothesized that vitamin D may reduce symptoms of **COVID-19** by suppressing cytokine storm in **COVID-19** patients.[43]

Vitamin D is produced in the bone, skin, lungs, colon, parathyroid glands, and immune system cells. Activation of vitamin D in response to viral infection has been described.[44] A deficiency of vitamin D could impair this response in the lung.[45]

4.4 Iodine

Iodine is an essential element; therefore it must be obtained from the diet or via supplementation. For over 40 years, US iodine levels have fallen in the National Health and Nutrition Examination Survey (NHANES).[46] Nearly 60% of women of childbearing age are deficient in iodine.[47] In fact, the mean urinary iodine concentration among pregnant US women is 134 ug/L which signifies deficiency.[48] We have tested over 6,000 patients and found the vast majority—over 97%– are deficient in iodine.

Iodine is needed for proper immune system functioning. Iodine supplementation has been shown to increased IgG synthesis in human lymphocytes.[49] Iodine deficiency is associated with decreased phagocytic activity of blood neutrophils.[50] This was associated with a decrease in peroxidases in neutrophils. Iodine has been shown to increase the ability of granulocytes to kill infectious organisms.[51] Iodine is used as an antiseptic throughout the US because it has antiviral and antibacterial properties. Two of us (DB and RN) have used iodine successfully as an antimicrobial agent for over two decades.

In order to reduce transmission of viruses, antisepsis of human and non-human surfaces must be identified. Researchers reported an *in-vitro* study where **SARS-2-CoV** was exposed to iodine (povidone-iodine) at 1-5% concentrations as a nasal antiseptic formulation and an oral rinse. The iodine solutions effectively inactivated **SARS-CoV-2** after exposure times of 60 seconds.[52] *In vitro* studies of 0.23% PVP-I mouthwash (1:30 dilution) was shown to inactivate both **SARS-CoV** and **MERS-CoV** following a 15-second exposure.[53]

Japan has one of the lowest rates of **COVID-19** illnesses in the Western world even in a crowded city such as Tokyo. Furthermore, Japan has not gone on a total lockdown. The Japanese are known to have a much higher iodine intake through their diet when compared to other Western countries. It is estimated that the Mainland Japanese ingest over 100x the RDA as compared to US citizens.[54] Perhaps Tokyo and Japan itself has had less serious **COVID-19** illness because of their iodine intake.

The full oral supplementation regimen (vitamins A, C, D, and iodine) in COVID-19 subjects was used in 91 out of 104 subjects in the cohort. The subjects were instructed to take the supplements for four days. Some were treated with vitamin C (1), vitamins C and D (2) and vitamins C, D, and io-

dine (1). All of these patients recovered without sequalae.

4.5 Nebulized Hydrogen Peroxide

If there were more serious problems or the oral supplementation regimen failed to fully help alleviate the symptoms of **COVID-19**, the next step was to initiate the use of a combination of nebulized hydrogen peroxide and iodine. A solution of 250 cc of normal saline was mixed with 3 cc of 3% hydrogen peroxide providing a final concentration of 0.04% hydrogen peroxide. (Note, the hydrogen peroxide used was initially a 35% food grade source then diluted to 3% using a 10:1 mixture of sterile water to 35% hydrogen peroxide.) Additionally, 1 cc of magnesium chloride (200 mg/ml) was added to the 250 cc saline/hydrogen peroxide bag. (This was mixed in the office for the patients.)

Patients were instructed to nebulize 3 cc of the mixture three times per day or more often if there were breathing problems. Usually one or two nebulizer treatments were reported to improve breathing problems.

A total of 91 **COVID-19** subjects (85%) utilized the nebulized solution. They reported no adverse effects. One We have been using nebulized saline/hydrogen peroxide at this concentration for over two decades in his practice.

Hydrogen peroxide is continually produced in the human body with substantial amounts produced in the mitochondria.[55] Every cell in the body is exposed to some level of hydrogen peroxide.[56] The lungs are known to produce hydrogen peroxide.[57] Nebulized hydrogen peroxide has been shown to have antiviral activities.[58] Hydrogen peroxide can activate lymphocytes[59] which are known to be depleted in **COVID-19**.

4.6 Intravenous and Intramuscular Therapies

If **COVID-19** patients continued to have symptoms such as shortness of breath, fever, or cough, they were offered intravenous injections of hydrogen peroxide, Vitamin C and intramuscular injections of ozone.

4.7 IV Hydrogen Peroxide

A dilute IV solution of hydrogen peroxide was given in either an IV drip over 30 minutes or a rapid infusion as an IV push over 2-3 minutes. One of the earliest known uses of hydrogen peroxide was used by Dr. T.H. Oliver in 1920. Dr. Oliver used IV hydrogen peroxide to treat Indian troops who were suffering from an influenza and pneumonia epidemic. The death rate was reported to be over 80% at that time. Dr. Oliver's results showed his IV hydrogen peroxide-treated cohort of 24 soldiers had a mortality rate of 48% compared to the 80% death rate from those treated with the usual care at that time.[60] In the article published by Dr. Oliver, he stated that the low oxygen symptoms his patients suffered from were markedly benefited by the use of intravenous hydrogen peroxide. Furthermore, he reported that the 'toxemia' (spread of bacterial products in the blood stream) appears to be overcome in many cases. Poor oxygenation and sepsis are both conditions experienced by **COVID-19** subjects.

When H_20_2 is produced extracellularly or added to a cell culture system, a gradient of H_20_2 is quickly established across the plasma membrane.[61] Researchers reported that the gradient is the result of H_20_2-scavanging enzymes including catalase and GSH-peroxidase that maintains a steady-state intracellular H_20_2 concentration being 10x less than the extracellular concentration.[62] As Bocci states, "This result is important because the intravenous (IV) infusion of a low and calculated concentration of H_20_2 results in a marked dilution in the plasma pool with partial inactivation and in intracellular levels able to exert biological effects on blood and endothelial cells without aggravating the concomitant oxidative stress."[63] **COVID-19** is known to cause oxidative stress which may be the cause of multi organ failure and hypoxemia.[64][65][66] H_20_2 is known to activate glycolysis, ATP and 2,3-DPG in red blood cells which can lead to improved oxygen delivery to ischemic tissues.[67][68] H_20_2 has also been shown to increase the production of NO which can aid in vasodilation and tissue oxygenation.[69][70]

Researchers studying the effects of intravenous H_20_2 therapy reported that it barely increases the

plasma level of peroxidation end-products (lipid oxygenation products). This stimulates the production of antioxidants which act as reducing agents. The scientists report similar effects with ozone therapy. This results in an up-regulation of antioxidant enzymes (SOD, GSH-peroxidase, G-6PD) in erythrocytes which has been demonstrated *in-vivo*.[71] Coronaviruses have been shown to be sensitive to oxidizing disinfectants such as a 0.5% hydrogen peroxide solution used as a surface disinfectant.[72] It is well accepted that the response of the immune system is the production of pro-oxidants which are known to disinfect pathogens.[73]

4.8 IV Vitamin C (Ascorbate)

Intravenous use of vitamin C has been used in hospitals and outpatient settings for **COVID-19** patients after a report from China showed improvement in those treated with it.[74] IV ascorbic acid was introduced to moderately to severely sick **COVID-19** patients in Chinese hospitals. The researchers reported that intravenous ascorbic acid provided safe and effective adjunctive care of hospitalized **COVID-19** patients. There was no mortality, no reported side effects and shorter hospital stays universally. The Shanghai expert group recommends intravenous ascorbic acid use in extremely critical settings within **COVID-19** patients. In the US, multiple hospital centers utilized IV vitamin C to treat **COVID-19** patients.

We have been successfully utilizing IV vitamin C therapies for over two decades in order to aid the immune system in its ability to fight pathogens. For this study, we administered 2.5 gm of sodium ascorbate mixed with 5 cc of sterile water as an intravenous push over 1-2 minutes. There were no adverse effects from this regimen.

4.9 Intramuscular Ozone

Ozone is a colorless gas with a pungent odor. It is a natural molecule made up of three atoms of oxygen. Ozone is produced by an ozone generator where oxygen (O2) gas is exposed to an electrical discharge combining O2 molecules into a mixture of up to 5% O3 and 95% O2. Ozone therapy has been used for over 100 years and is widely used in Europe and Cuba and in outpatient offices in the United States. Ozone has been used to treat infections and wounds as well as other illnesses over this time period. Ozone therapy can be administered by many different methods including intravenously and intramuscularly. Intramuscular ozone was given in these cases to reduce transmission risk. Since we were only treating **COVID-19** patients outside the office in the parking lot, intramuscular injections of ozone were deemed the easiest and safest modality.

IM ozone was provided to 37 patients (35%). Of these, a single ozone injection was given to 31 (82%). Seven (18%) required more than one IM injection. Five received two ozone shots, one patient had four and another had six. The patients who required four and six injections had been ill for a longer time period (over 10 days) before instituting therapy. Both recovered uneventfully. In viral infections, ozone has been shown to improve both the innate and adaptive immune systems while also reducing cytokine storm. Ozone improves neutrophil counts in children with compromised phagocyte cell-mediated immunity.[75] Antibodies have been shown to kill pathogens by producing ozone gas.[76] Ozone has been shown to have direct viricidal effects by disrupting the lipid envelope of a virus at sites of double bonds. When the lipid envelope is fragmented, its DNA or RNA cannot survive. **SARS-CoV-2** is an enveloped virus which would make it an excellent candidate for treatment with ozone.[77] Furthermore, **SARS-CoV-2**, as well as other coronaviruses, have abundant cysteine–a thiol containing amino acid– in their spike proteins. Rowen has hypothesized that ozone is the ideal therapy for viruses.[78] In order to successfully penetrate cell membranes, many viruses require membrane glycoproteins to be in the R-S-H reduced form as opposed to the oxidized—R-S-S-R– form. If virus thiol groups are oxidized they lose infectivity.[79] Rowen states, “Creating a more “oxidized” environment may allow ozone therapy. . . to assist the body in inactivating thiols in viruses in blood and tissues.” **SARS-CoV-2** cell entry spike proteins are particularly rich in both cysteine and tryptophan the two most vulnerable

amino acids to alteration by ozone.[80][81] The thiol group of cysteine is easily oxidized reversibly to disulfide which is widely accepted to neutralize the function of its protein/enzyme. Effectively, it is an "on-off" switch. Potent oxidants, such as hydrogen peroxide or ozone, can irreversibly oxidize the thiol. Regardless, viruses have no means to self-repair even when in the disulfide oxidation state. Regarding tryptophan, its electron rich indole group is very vulnerable to irreversible oxidation, even by hydrogen peroxide.[82] Ozone, like ascorbate, has been shown to increase the production of hydrogen peroxide.[83][84] This viral redox vulnerability theory was verified with the use of ozone rapidly remitting 100% of 5 cases of Ebola in 2014. The Ebola virus similarly has a large quantity of cysteine in its membrane glycoproteins.57 **COVID-19** is associated with microthrombotic events and, often, a cytokine storm of inflammation. Ozone could be particularly useful as it improves the prostacyclin:thromboxane ratio and enhances nitric oxide production.[85] Ozone has been shown to reduce production of TNF-α[86] as effectively as steroids do and increases the production of the anti-inflammatory enzyme heme oxygenase-1.[87] Ozone treatment also induces *Nrf 2* phosphorylation, which has been reported to reduce oxidative stress and proinflammatory cytokines in multiple sclerosis patients, and, in low doses.[88] *Nrf 2* is a regulator of genes related to antioxidant responses.[89] The limitations of this study include that most patients were taking nutritional supplements before they became ill. Therefore, they may have had fewer nutritional deficiencies compared to the average American. Furthermore, the majority of the subjects in this study, which mirrored the practice, were women. As compared to women, more men die of **COVID-19**.[90] Hypertension, diabetes, and obesity are known co-morbidities with **COVID-19**.[91] Our patient population had lower rates of these illnesses when compared to US averages. Since this was not a randomized, double-blind, placebo-controlled study, the therapies provided here cannot be proven to cure the symptoms of **COVID-19**. The observations of the positive outcomes are supported by this consecutive case series even without a control group. During the **COVID-19** pandemic, we felt that it was not ethical to use a control group and withhold treatment from ill **COVID-19** patients.

Case control series have been shown to play an important role in evidence generation and in clinical practice.[92] The author of the fore worded report, Cynthia Jackevicius states, "Who better than clinicians—who are the first to see how new therapies are being used and how patients respond to the new therapies—to share their valuable insights and experience in the medical literature through the use of case reports? A fundamental tenet of evidence-based clinical practice is to use the best available clinical evidence, and at times, a case report or case series is the best available evidence to guide decision-making."

Additionally, the results of this study offer a new consideration for the current medical study paradigm, which generally evaluates a single agent (or occasionally more) against a disease or pathogen. Considering the very favorable outcome of our consecutive case cohort (no deaths, only one hospitalization in patients treated prior to admission, and rapid recovery), this work supports an alternate paradigm for infection and medical challenges: providing support of the body's biochemical/nutritional needs and augmenting its innate physiological defense responses. Every substance used in our cohort is either an essential nutrient or an oxidant mediator actually manufactured by the body. Nothing foreign to the body was used, nor anything patentable. The disparity in the health outcomes under our treatment protocol and the outcomes in the rates of serious and critical illness and death under other protocols is stark and demands further investigation.

5. Conclusion

In summary, we treated 107 COVID-19 patients, solely with biological therapies, who all recovered. Only three were hospitalized. Of the three hospitalizations, two were hospitalized before beginning our treatment and sought our care post hospitalization. One was hospitalized while solely taking the oral regimen of Vitamins A, C, D, and iodine, and

not the oxidative therapies. All recovered uneventfully. There were no deaths.

In the state of Michigan, as of 6/21/20, the case fatality rate was 9.0% (6,067 deaths and 67,097 positive cases of SARS-CoV-2). [92] Therefore, out of our 107 COVID-19 patients, 10 deaths could be predicted. At the very least, with 25 patients testing positive for the virus, we should have expected two deaths, but in reality, we should have seen significantly more morbidity considering we only had 33 tests performed on the 107 patients (all symptomatic), a median age of 56, and comorbid conditions. Of the 107 patients total, we should have experienced at least eight hospitalizations considering the median age, according to a published analysis. [93]

As of this publication, no cure, treatment, or preventive for SARS-CoV-2 has yet been proven effective in a randomized study, except for dexamethasone (a potent steroid) use in severely ill, hospitalized patients. In this study a novel treatment program, which is hypothesized to aid and support the immune system, was highly effective in the re-covery of 100% of 107 patients. This case review points out that specific and relatively inexpensive nutritional support along with oxidative intravenous as well as intramuscular, and nebulized oxidative solutions may be helpful for COVID-19 patients. Future, randomized studies are needed to elucidate the effectiveness of this or similar regimens.

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***Editor's Erratum Note, 7/9/2020, 8:20PM**
Due to a typographical error, the amount of Vitamin A in the protocol was originally reported as 10,000 IU/day. The correct value should have been 100,000 IU/day.