
Christof Plothe DO
Covid 19
health promotion protocol
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Disclaimer

The recommendation below results from over two years of exchange with health care practitioners from all over the world as well as personal experience gained from treating hundreds of patients; it is also based on scientific insights from brave and inquisitive people in the medical profession. The advice given is to concentrate on key factors influencing the progression of Covid-19 infection. The current approach is much simplified in comparison with past protocols, to allow each individual to choose a health-promoting method in the event of infection. Adequate Vitamin D levels and avoidance of sugar (grains) seem to be the single most important elements determining the progression. Studies and real-life cases have shown that elevation of glucose levels can facilitate the progression of the disease through multiple mechanisms. This can explain much of the difference in disease severity seen across the population ****. With Vitamin D, a theoretical point of zero mortality is achieved at approximately 50 ng/mL D3 *****. Quercetin, a so-called ionophore, has been shown to help Zinc to elicit its solid antiviral potential (See appendix). NAC has demonstrated its ability to interfere with many metabolic stages of the virus ******. Always ask your doctor to include elements of the various existing protocols used e.g. the one published by the FLCCC*.

We recommend that these measures be included in any highly effective current Covid-19 treatment protocol*. Please also check the appendix and references below for more information. Unfortunately, these protocols are still not included in the official guidelines of most countries. We recommend stocking these supplements/medications in advance so you may start as early as possible in the event of infection.

Early intervention is essential. Please always consult your doctor when symptomatic and starting a protocol.

Prevention

Vitamin D

Please get your Vitamin D levels checked regardless of the season and your supplementation. The ideal value should be between 50 and 80 ng/ml *****. Make sure you are in this range by repeating the measurement after three weeks if not achieved in the first analysis.

Diet

Make sure there are enough vegetables, fruit, and legumes on your table every day **.

Exercise

Make sure you get some daily physical activity, preferably outdoors and in unpolluted conditions.********

In the event of symptoms, include the following as support for an adult :
Minimum Supplementation

- Vitamin D 10 000 IU a day
- Quercetin 2 x 500 mg a day together with
- Zinc 2 x 30 mg a day
- NAC 3 x 600 mg
- Nasal spray (NO, Hydrogenperoxide 3 % diluted, povidone iodine 1%)*******

(Please look at the list of additional suggestions in the appendix)

Diet (Of primary importance)

- **Refrain 100 % from consuming grains** (bread, pasta, müsli, etc.) and **sugar** ***
- Avoid animal proteins (dairy and meat)
- Avoid fats/oils
- Include loads of vegetables, fruit (not as juice), and legumes

* i.e. FLCCC protocol: https://covid19criticalcare.com/covid-19-protocols/
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***** Borsche L, Glauner B, von Mendel J. COVID-19 Mortality Risk Correlates Inversely with Vitamin D3 Status, and a Mortality Rate Close to Zero Could Theoretically Be Achieved at 50 ng/mL 25(OH)D3: Results of a Systematic Review and Meta-Analysis. Nutrients. 2021 Oct 14;13(10):3596. doi: 10.3390/nu13103596. PMID: 34684596; PMCID: PMC8541492.
****** Du Preez H, Aldous C, Hendrik, Kruger G , Lin J; N-acetylcysteine and other sulfur-donors as a preventative and adjunct therapy for COVID-19, to be published in Advances in Pharmacological and Pharmaceutical Sciences Journal July 2022 https://doi.org/10.1155/1970/4555490
******* https://covid19criticalcare.com/covid-19-protocols/i-care-early-covid-treatment/-includes instruction for how to make a 1% povidone-iodine solution; https://www.tribuneindia.com/news/health/nasal-spray-lowers-covid-viral-load-by-94-per-cent-in-24-hours-lancet-study-412372?utm_source=substack&utm_medium=email
******** https://bjsm.bmj.com/content/early/2022/07/07/bjsports-2022-105733

Appendix and References for Protocol:

Gentics in Covid-19 Patients

Researchers on the genomics of severe covid-19 progression identified robust genetic signals relating to key host antiviral defence mechanisms, and mediators of inflammatory organ damage in Covid-19. Both mechanisms may be amenable to targeted treatment with existing drugs. They found evidence in support of a causal link from low expression of IFNAR2, and high expression of TYK2, to life-threatening disease; transcriptome-wide association in lung tissue revealed that high expression of the monocyte/macrophage chemotactic receptor CCR2 is associated with severe Covid-19 (Pairo-Castineira, 2020).

Blood groups

Many viral diseases have shown an association with ABO blood groups in the past. SARS-CoV, being one of them, showed a positive association with blood group A with a high number of positive cases in blood group A. Blood group O, on the other hand, had a lesser incidence of infection compared with other groups (Zaidi, 2020).

Exercise

PGE2 production, either induced by SARS-CoV-2 infection or determined by endogenous and exogenous risk factors critically influences COVID-19 disease severity. In conclusion, SARS-CoV-2, male sex, old age, and sedentary life style increase PGE2 levels, which may reduce the early anti-viral defense as well as the development of immunity promoting severe disease courses and multiple infections. Regular exercise and Taxifolin (Larch tree) treatment may reduce these risks and prevent severe disease courses (Ricke Hoch, 2021).

Nutrition

Given the profound public health concerns related to the current COVID-19 pandemic, modifiable risk factors for developing severe and critical complications are urgently needed, especially ones that may be easily implemented and nutritionally based (Asher, 2021). As it was stated above, the "terrain" and therefore the state of the cell environment is essential for a healthy cell. The basis for the right electrolyte distribution, pH, micronutrient supply, etc. is our nutrition, so it should the basis of all treatments. Specific studies of malnutrition and the loss of viral defense (Ritz, 2006) stress the importance of dietary factors in Covid-19 infection. There is no single food or natural remedy that has been proven to prevent COVID-19 infections, nor is there such a drug; this has been made clear by the WHO (WHO, 2020b). However, learning from previous research into other viral infections, it is clear that nutritional status plays a significant role in patient outcomes (Beck, 2004). Now more than ever, wider access to healthy foods should be a top priority and individuals should be mindful of healthy eating habits to reduce susceptibility to and long-term complications from COVID-19 (Butler, 2020). The high rate of consumption of diets high in saturated fats, sugars, and refined carbohydrates (collectively called the Western Diet, WD) worldwide, contribute to the prevalence of obesity and type 2 diabetes, and could place these populations at an increased risk for severe COVID-19 pathology and mortality (Butler, 2020).

In Covid-19 it is essential to supply the body with the right micronutrients, to support the microbiome and not trigger a proinflammatory response whilst supporting the immune system. Zabetakis et al. (Zabetakis, 2020) stress the importance of nutrition as a mitigation strategy to support immune function amid the COVID-19 pandemic, identifying food groups and key nutrients of importance that may affect the outcomes of respiratory infections. Blanco-Melo et al. (Blanco_Melo, 2020) determined that the unique inappropriate inflammatory response of COVID-19 is due to the low levels of type I and II interferons in conjunction with an elevated expression of IL-6 and increased chemokines. They hypothesize that the enhanced inflammatory response, along with a reduced innate antiviral defense, may be the "defining and driving feature" of COVID-19 infections. A diet should therefore address these two areas: supporting cellular defense whilst calming inflammation. Generally, where possible, an effective strategy to reduce one's risk of developing severe Covid is to control the activities of inflammatory mediators via modifiable risk factors such as diet, exercise, and healthy lifestyle choices (Tsoupras, 2008; Yu, 2018). Only the adoption of a long-term and consistent dietary pattern benefits human health. Conversely, adoption of an unhealthy diet and lifestyle is associated with low-grade inflammation and increased oxidative stress, which could lead to the development of co-morbidities associated with more severe Covid-19 outcomes (Tsoupras, 2008; Wu, 2020). Certainly, there is considerable evidence that the food and nutrients we consume affect how our immune systems function (Childs, 2019;

Chandra, 1996; Hulsewé, 1999). It is particularly important at this time to consider our elderly communities, as the elderly are vulnerable to the increased risk of malnourishment, infections, and COVID-19 (CDC, 2020b). This is due to a functional decline of the immune system with age known as immunosenescence (Pae, 2012; Meyer, 2010). Malnourishment can occur for several reasons, including poor socioeconomic conditions, mental status, social status, and a host of other multifactorial issues (Volkert, 2020). Indeed, often, there are nutritional deficiencies of calcium, vitamin C, vitamin D, folate, and zinc amongst elderly populations (Power, 2014).

While COVID-19 affects all groups, severe pathology and mortality is disproportionately highest, as mentioned, in the elderly, underrepresented minorities (Blacks/African Americans and Latinos), and/or in those with underlying comorbidities. Obesity and type 2 diabetes, two prominent risk factors for severe Covid-19, may underlie the health disparity observed in these populations (Dietz, 2020, Dharmasena, 2016). The high prevalence of these risk factors, worldwide, but especially in the U.S. and other developed countries, is likely driven by increased consumption of the typical Western diet (WD) consisting of high amounts of saturated fat (HFD), refined carbohydrates and sugars, and low levels of fiber, unsaturated fats, and antioxidants (Cordain, 2005).

Fruit and Vegetables

The basis for many beneficial micronutrients and phytochemicals should be fruit and vegetable consumption. Fruit and vegetable intake has been investigated for potential benefits in association with respiratory (Kaluca, 2018) and inflammatory (Holt, 2009) conditions due to their nutrient profile consisting of antioxidants, vitamins, minerals, and phytochemicals containing phenolic compounds that can exert antioxidant, anti-inflammatory, and other beneficial effects (Cheng, 2017; Serino, 2018; Lichota, 2019). Indeed, polyphenols may also exhibit antiviral effects against the West Nile virus, Zika virus, and Dengue virus (Jasso-Miranda, 2019; Vázquez-Calvo, 2017).

Nightshades and Lectin-rich Vegetables

Certain vegetables, especially nightshades (Solanaceae) such as tomatoes, potatoes, peppers and eggplant contain so called lectins, as do certain nuts and seeds including cashews, peanuts, pumpkin, and sunflower seeds, grain-fed and farm-raised animal proteins, beans and legumes and A1 dairy products as well. Whilst these are all healthy foods they can promote inflammation and should be fermented prior to eating. In order not to increase the histamine content, histamine-lowering probiotics should also be used.

Sugar, Grains and Flour

A machine-learning model was developed to interpret 240,000 scientific articles openly accessible in the Covid-19 database, and construct knowledge graphs to synthesize the extracted information and navigate the collective knowledge in an attempt to search for a potential common underlying reason for disease severity. The machine-driven framework we developed pointed repeatedly to elevated blood glucose as a key facilitator in the progression of Covid-19. Indeed, when the researchers systematically retraced the steps of the SARS-CoV-2 infection, they found evidence linking elevated glucose to each major step of the lifecycle of the virus, progression of the disease, and presentation of symptoms. Specifically, elevation of glucose provides ideal conditions for the virus to evade and weaken the first level of the immune defense system in the lungs, gain access to deep alveolar cells, bind to the ACE2 receptor and enter the pulmonary cells, accelerate replication of the virus within cells, increasing cell death and inducing a pulmonary inflammatory response, which overwhelms an already weakened innate immune system to trigger an avalanche of systemic infections, inflammation and cell damage, a cytokine storm and thrombotic events. They tested the feasibility of the hypothesis by manually reviewing the literature referenced by the machine-generated synthesis, reconstructing atomistically the virus at the surface of the pulmonary airways, and performing quantitative computational modeling of the effects of glucose levels on the infection process. They conclude that elevation in glucose

levels can facilitate the progression of the disease through multiple mechanisms and can explain much of the differences in disease severity seen across the population. The study (Logette, 2021) provides diagnostic considerations, new areas of research and potential treatments, and cautions on treatment strategies and critical care conditions that induce elevation in blood glucose levels.

Grains theoretically contain many healthy nutrients but keep them chelated by phytic acid so we cannot use them properly. Fermentation, e.g. using the sourdough method, reduces the content of phytic acid, making the micronutrient more available (Gabriele, 2019), which can support our immune system. Grains also contain a variety of lectins (i.e. gluten), which can trigger a proinflammatory response in our gut (Brouns, 2019). Refined flour can also add to a proinflammatory state by altering the gut microbiome (Spreadbury, 2012). It also adds to weight thereby increasing the number of fat cells (Ryan, 2019), which are heavily supplied with ACE 2 receptors. This can help more Covid viruses to enter the cells, thus increasing the overall viral load. The avoidance of grains and sugar is an essential part of a Covid-19 treatment approach.

Oils

Whilst Omega 6 oils (Calder, 2017) and saturated fats (Fritsche, 2015; Rogero, 2018) show a proinflammatory effect and thus should be avoided, there is the potential that Omega 3 oils like EPA, DHA (Yan, 2013; Calder, 2015), and other dietary unsaturated fatty acids (Arachidonic acid) can inactivate enveloped viruses and decrease inflammation. It is thought that these fatty acids and others cause leakages or lysis of the viral envelopes by disrupting the membrane integrity, amongst other potential mechanisms (Das, 2020; Hilmarrson, 2006). Indeed, when challenged by viruses, including SARS-CoV-1, MERS, and, potentially, SARS-CoV-2, alveolar immune cells such as macrophages, leukocytes, natural killer cells, and B and T cells release unsaturated fatty acids such as AA into the surrounding microenvironment (Das, 2020). Notably, an in-vitro model of human cells (Huh-7 and VeroE6) infected with a human coronavirus (HCoV-229E) demonstrated that several bioactive lipids downstream of phospholipase A2 (PLA2) activation were upregulated by the host cells. It is postulated that coronaviruses modulate the host lipid profile to optimize and maintain a specific homeostasis for viral replication. However, exogenous supplementation of AA and linoleic acid suppressed viral replication by interfering with the optimal host lipid conditions for viral replication. Notably, exogenous supplementation of AA and linoleic acid was also conserved when human cells were infected with MERS [166]. EPA, DHA, and AA also inhibited the replication of enterovirus A71 and coxsackie virus A16 (Yan, 2019). This suggests that AA, EPA and DHA and their anti-inflammatory metabolites such as lipoxin A4, resolvins, protectins and maresins, function as endogenous anti-microbial molecules and so their appropriate use may aid in decreasing morbidity and mortality induced by SARS-CoV-2, SARS and MERS (Das, 2020).

Omega 3 Fatty Acids

Very-long chain omega-3 fatty acids (EPA and DHA) have anti-inflammatory properties (Manzanres, 2019; Husson, 2016; Schulze, 2016; Hozawa, 2006) that may help reduce morbidity and mortality from COVID-19 infection (Asher, 2021; Panigraphy, 2020; Panday, 2020; Well, 2020; Su, 2020; Egea, 2020; Rogero, 2020; Brenna, 2020). Multiple randomized clinical trials (RCTs) are currently (as of January 2021) underway testing the hypothesis that treatment with omega-3 fatty acids (EPA and DHA) will have beneficial effects on a variety of aspects of COVID-19 infection. Although their outcomes are not yet known, there are compelling scientific reasons to expect that these studies will be positive (Asher, 2021).

Fiber

As our western diet creates deficiencies of fiber (Alcenar, 2020) and fiber intake has been associated with gut (Holscher, 2017) and microbiome (Holscher, 2017) function, an increase in fiber is recommended. Studies demonstrate a lower incidence of bacterial translocation across the gut barrier with the administration of dietary fiber (Schley, 2007), suggesting that this nutrient modulates immunity. Among the potential

mechanisms by which dietary fiber influences the immune system are changes to the gut-associated lymphoid tissues (GALT) arising from altered gut microflora (Microbiome). Prebiotic fiber is neither hydrolyzed nor absorbed in the upper part of the gastrointestinal tract and becomes a selective substrate for one or a limited number of beneficial colonic bacteria (Arrieta, 2011; Roberfroid, 2010)]. Indeed, fiber intake has been shown to increase the survival of influenza-infected mice via various mechanisms, including blunting the immune response by altering the type of immune cells generated and the generation of diet-derived short-chain fatty acid (SCFA)-enhanced CD8+ T cell effector functions by altering the cell's metabolism (Trompette, 2018). Western diets are often deficient in dietary fiber (Alcenar, 2018); increasing the consumption of both soluble (oat bran, barley, nuts, seeds, beans, lentils, peas, and some fruits and vegetables) and insoluble (wheat bran, vegetables, and whole grains) sources of fiber to the recommended 25–38 g/day is therefore advisable (King, 2012). Currently, there are no recommendations for fiber intake during the pandemic.

Meat and Dairy Products

Evidence has shown that pigs and rabbits can be infected by SARS-CoV-2. Slowly knowledge is accumulating that more animals might be infected. Viral transmission through meat and dairy products may therefore be conceivable, indicating carry-through contamination (Yekta, 2020). This could be a big factor for the meat industry where large quantities of animals live in close proximity to each other. Cats, ferrets, minks, pangolins, snakes and turtles have been postulated as intermediate hosts of the novel coronavirus (Ji et al. 2020; Li et al. 2020; Nabi et al. 2020; Wu et al. 2020). He (He, 2020) et al. show that COVID-19 transmission from humans to animals is likely to amplify mutations and, in turn, re-infect humans with deadlier mutants. As covid-19 uses the ACE2 receptor to enter a cell and ACE2 receptors are found in over 400 vertebrate species including both domestic and wild animals (Damas, 2020; Wu, 2020), this aspect should be monitored carefully. Dairy products and modern meat production contain much more saturated fat than in the past so a proinflammatory effect from animal products can be expected. Studies have shown that a single meal of meat, dairy, and eggs triggers an inflammatory reaction inside the body within hours of consumption (Greger, 2012). The high bacteria load in raw or cooked animal foods may trigger an endotoxemic surge of inflammation, potentially exacerbated by the presence of saturated animal fat.

Prebiotics

Apples, Artichokes, Asparagus, Bananas, Barley, Berries, Chicory, Cocoa, Dandelion greens, Flaxseed, Garlic, Green vegetables, Konjac root, Leeks, Legumes (aka Pulses, e.g. peas, beans), Oats, Onions, Tomatoes, Soybeans, Wheat and Yacon root are foods that are known to support heatlthy gut bacteria and should be included daily. Some experts say you should get at least 5 grams of prebiotics in your diet every day. Care should be taken if patients have Irritable Bowl Syndrome (Sinagra, 2017) or small intestinal bacterial overgrowth, called SIBO (Losurdo, 2020), or FODMAPs (Hill, 2017) intolerance.

Diet Summary

Diet could be one of the most underestimated factors affecting the progression of a Covid-19 infection. Nutrient intake and an antiinflammotory effect whilst supporting the microbiome are crucial factors determining the balance between health and disease. It is therefore recommended that individuals refrain from eating foods high in saturated fats and sugar and instead consume high amounts of fiber, fermented whole grains (sourdough), unsaturated fats, and antioxidants to boost immune function (Connaughton, 2016). In times of infection, plant-based nutrition can prove a crucial anti-inflammatory factor. Lectin-rich foods should be neutralized so as not to promote inflammation. Prebiotics should be included to serve the important gastrointestinal microbiome. This is especially important in the elderly as studies can prove the immune-nutrition interplay in aging (Alam, 2019).

Microbiome

The human microbiome is the aggregate of all microbiota that reside on or within human tissues and biofluids along with the corresponding anatomical sites in which they reside. Our recent understanding that the human body supports a thriving diversity of microbial life has led to a greater appreciation of the expanded functional gene capacity of the human superorganism (Rackaityte, 2020). The microbiota plays a fundamental role in the induction, training and function of the host's immune system (Belkaid, 2014). What is becoming more apparent is that a wide array of conditions, ranging from chronic inflammatory (Arrieta, 2014; Fujimura, 2016) and metabolic diseases to neurological disorders and cancer have now been associated with microbiome functional perturbations. The microbiome consists of microbes that are both helpful and potentially harmful (Ursell, 2012). Most are symbiotic (where both the human body and the microbiota benefit) and some, in smaller numbers, are pathogenic (promoting disease). In a healthy body, pathogenic and symbiotic microbiota coexist without problems, but if there is a disturbance in that balance—brought on by infectious illnesses, certain diets, or the prolonged use of antibiotics or other bacteria-destroying medications—dysbiosis occurs, stopping these normal interactions. As a result, the body may become more susceptible to disease. Gut microbiome composition was significantly altered in patients with COVID-19 compared with non-COVID-19 individuals, irrespective of whether patients had received medication (Yeoh, 2020). The researchers said patients with severe illness exhibit high blood plasma levels of inflammatory cytokines and inflammatory markers — and that given altered gut microbiota composition in SARS-CoV-2 infected subjects, there is substantial involvement of the GI tract during infection. These results suggest that gut microbiota composition is associated with the magnitude of immune response to COVID-19 and subsequent tissue damage and thus could play a role in regulating disease severity. The scientists also found that because a small subset of patients showed gut microbiota dysbiosis, or imbalance, even 30 days after recovery, this could be a potential explanation for why some symptoms persist in what is known as long COVID (Zuo, 2020). The virus may also cause epithelial barrier dysfunction, enhancing damaging inflammatory responses. Dysbiosis in the gut, nose, oropharynx and lungs may initiate and worsen these pathogenic processes. The well-known comorbidities of COVID-19 are all associated with dysbiosis. On the other hand, healthy microbiota may inhibit the development of excessive inflammation and enhance an effective immune response, leading to better outcomes. Preventive and treatment strategies can be developed to enhance the health of our microbial populations, improving results (Friedland, 2020). Given the intricate influence of gut microbiota (GM) on host immune effectors and subsequent inflammatory profile, GM composition and function might contribute to explaining the individual resilience/fragility with respect to COVID-19 and/or the response to therapeutics; this deserves further research (Ferreira, 2020). A newly-formed Microbiome Centers Consortium (MCC) identified four ways to leverage the strengths and experience of microbiome centers in the response to the COVID-19 pandemic. To meet these needs, the MCC will provide a platform for coordinating clinical and environmental research, assisting with practical obstacles, and helping to communicate the connections between the microbiome and COVID-19 (MBC, 2020). A recent article even proposed a lower mortality rate in Covid-19 when a healthy microbiome is present (Janda,2020).

Microbiome Summary

In conclusion, intestinal microbiome dysbiosis, which often occurs in the elderly, obese people and those with underlying chronic disease, may be responsible for a higher case fatality ratio (CFR). The microbiome, the last discovered organ of the human body, seems to be a significant factor that plays a major role in the COVID-19 epidemic. An unconscious approach to microbiome care in the form of daily supplementation of postbiotics in the form of fermented foods may explain this epidemiologically significant difference in the course of the disease (Janda, 2020).

NO (Nitric-oxide)

A hallmark of endothelial dysfunction and thrombotic events is suppressed endothelial nitric oxide synthase (eNOS) with concomitant nitric oxide deficiency (Green, 2020). Restoring nitric oxide, independent of eNOS, may counter endotheliitis and contribute to pulmonary vasodilation, antithrombotic, and direct antiviral activity in Covi-19 (Green, 2020). As to the latter, nitric oxide reportedly interferes with the interaction between coronavirus viral S-protein and its cognate host receptor, ACE-2. Nitric oxide-mediated S-nitrosylation of viral cysteine proteases and host serine protease, TMPRSS2, which are both critical in viral cellular entry, appear to be nitric oxide sensitive (Akerstrom, 2019; Sura, 1999; Hoffman, 2020; Arora, 2018; Shulla, 2011). Martel and colleagues provide a thoughtful review on strategies to increase airway nitric oxide to treat and possibly prevent Covid-19 (Martel, 2020). Paranasal sinuses continually produce nitric oxide (NO), a reactive oxygen species that diffuses to the bronchi and lungs to produce bronchodilatory and vasodilatory effects. Studies indicate that NO may also help to reduce respiratory tract infection by inactivating viruses and inhibiting their replication in epithelial cells. Based on a report of improved lung function during the 2003 SARS outbreak, the FDA's emergency expanded use of nitric oxide gas is now underway for treating Covid-19 (Martel, 2020). Alternatively, dietary inorganic nitrate has been shown in multiple studies to be effective at restoring endothelial function, reducing pulmonary and arterial hypertension, and promoting antimicrobial activity (Green, 1995). It is well understood that dietary inorganic nitrates (Beetroot, rhubarb, spinach, celery, lettuce and rucola, etc.) is bio-converted to nitric oxide through a series of well-defined steps beginning with the friendly microflora on the tongue reducing nitrate to nitrite, which is subsequently reduced to nitric oxide in the gut, bloodstream, and various organs, including the lung. The formation of inorganic nitrite and S-nitrosothiols is absorbed into the circulation where it acts as a transitory storage pool for subsequent nitric oxide production (Lundberg, 2015). The conversion of inorganic nitrite to nitric oxide is expedited in conditions of acidosis or hypoxemia, which occurs in regions of the pulmonary vasculature in the lungs of COPD patients and those who exhibit acute respiratory distress syndrome as observed in coronavirus infected lungs. Reportedly, consumption of inorganic nitrate for 8 days in a COPD population increased lung nitric oxide by 200% and reduced respiratory symptoms (Nagaki, 1995; Nathan, 1994). Restoring nitric oxide through dietary inorganic nitrate may be a consideration for prevention and early treatment which would operate at two-levels: reverse platelet-endothelial dysfunction and associated thrombosis as well as lower viral burden (Martel, 2020; Green, 1995; Lundberg, 2015; Green, 1993; Behina, 2018), and additionally could assist in opening airway passages. Other studies suggest that therapies designed to increase airway NO levels via gas inhalation and donor molecules (A nasal spray has been developed in Israel and Canada) may improve oxygenation and produce health benefits in COVID-19 subjects. In addition, limiting the lifestyle factors that reduce endogenous NO levels in the airways—such as mouth breathing and smoking—may also help to reduce the SARS-CoV-2 viral load and symptoms of COVID-19 pneumonia by promoting more efficient antiviral defense mechanisms in the respiratory tract. In the absence of effective treatments targeting SARS-CoV-2, we believe that these strategies should be considered and tested to mitigate the symptoms of COVID-19. Finally, the overall severity of disease would also be decreased by combining nasal breathing with a healthy lifestyle that includes exercise, a full night's sleep, and a balanced diet (Martel, 2020).

Vitamin C

Vitamin C has been used in antiviral approaches for many years (Colunga Biancatelli, 2019; Sorice, 2014; Maggini, 2012). Early after the occurance of Covid-19, high dosages of vitamin C have been used in many treatment protocols all over the world (Esp. China), unmentioned by the WHO and western medical systems (Abobaker, 2020). Coronaviruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza viruses increase oxidative stress in the body leading to cellular and tissue damage. To combat this, administration of high-dose vitamin C (ascorbic acid or ascorbate), in addition to standard conventional supportive treatments, has been shown to be a safe and effective therapy for severe cases of respiratory viral infection (Hoang, 2020). Many mechanisms for its potential benefit in Covid -19 have been reported

(Gonzales, 2020). It can cause damage of the viral capsid due to ascorbic acid redox capacity when given in pharmacological doses. Ascorbic acid is a powerful reducing agent (Cheng et al. 2012; Furuya et al. 2008). It can lead to disruption of viral capsid sugar variety of its glycoprotein envelope when given in pharmacological doses (Asim et al. US20130004458A). It can cause inhibition of viral replication when provided in pharmacological doses by creating a hostile environment for this activity to occur, in addition to directly inhibiting viral replication enzymes (Colunga Biancatelli et al. 2020; Kim et al. 2013; Jariwalla & Harakeh, 1996). Ascorbic acid causes degradation of single and double-stranded genomes of RNA and DNA viruses (Murata & Kitagawa, 1973; Murata & Uike, 1976; Wong et al. 1974) so that replication becomes susceptible to ascorbate-mediated damage, resulting in reduced viral protein production. It increases cellular immunity by increasing the number, activity, and aggressiveness of immune cells such as leukocytes, lymphocytes, NK cells, macrophages. Lymphocyte function and production are influenced by vitamin C concentrations (Sorice et al. 2014). Vitamin C accumulates in the lysosomes of phagocytic cells and enhances chemotaxis, chemokinesis and phagocytosis. Vitamin C in the presence of oxygen favors the generation of reactive oxygen species such as H2O2 (Frei & Lawson, 2008). Vitamin C has been shown to increase the mobility and chemotaxis of phagocytes (Murata & Uike, 1976). White blood cells accumulate vitamin C against a concentration gradient, resulting in values that are 50- to 100-fold higher than plasma concentrations (Goldschmidt, 1991; Bergsten et al. 1990; Evans et al. 1982). It increases humoral immunity through the production of antibodies (Carr & Maggini, 2017; Tanaka et al. 1994; Feigen et al. 1982). It increases anti-viral proteins such as α/β interferons while downregulating the production of the pro-inflammatory cytokines TNF-α and IL-6 (Colunga Biancatelli et al. 2020; Wintergerst et al. 2006; Dahl & Degre, 1976). It increases energy by providing necessary electrons and electron movement that increases mitochondrial electron flux for ATP generation (Gonzalez et al. 2005, Gonzalez et al. 2010). It limits glucose utilization as the main source of energy pathogenic organisms, when provided in pharmacological doses (Dakhale et al. 2011, Sanchez 2015; Ripoli et al. 2010). DNA and RNA viruses are able to induce glycolysis. Viruses are able to decrease host cell oxidative phosphorylation and increase dependence on extracellular glucose. Antioxidant action is elicited when vitamin C is provided in proper doses to prevent the dangerous and severe pathological cascade of the cytokine storm (Carr & Maggini, 2017; Marik 2018a; Marik 2018b; Hickey et al. 2005; Marik, 2016). It mitigates the cytokine storm – cytokines can elicit pro-inflammatory or anti-inflammatory responses, and Vitamin C appears to modulate systemic and leukocyte-derived cytokines. Vitamin C protects the host cells against the oxidants released by phagocytes. Vitamin C decreases the generation of the pro-inflammatory cytokines TNF-α and IL-6 (Chen et al. 2014). The lethal pathology underlying COVID-19 is acute lung injury (ALI)/acute respiratory syndrome (ARDS) induced by cytokine storm or significantly elevated oxidative stress. These pathologies were also found in SARS and MERS and other respiratory viral infections, as well as viruses affecting other parts of the body causing multi-organ failure. The clinical observations of vitamin C in ameliorating pneumonia, ARDS and sepsis, support vitamin C's antioxidant, anti-viral, and immune-boosting effects. It maintains the structural integrity of cells via the promotion of collagen formation (Englard & Seifter, 1986; Murad et al. 1981). Vitamin C protects endothelial barrier function against the insult of sepsis (Han et al. 2010). It modulates gene expression. Vitamin C administration decreases the expression of susceptibility genes, including mitochondrial antiviral signaling (MAVS) and interferon regulatory factor 3 (IRF3), and increases the expression of NF-κB. These in conjunction induce type I interferons (IFNs) and elicit innate antiviral response (Cai et al. 2015). High-dose vitamin C treatment acts as both a pro-oxidant for immune cells, and an antioxidant for lung epithelial cells (Erol, 2020). The pro-oxidant role of vitamin C requires pharmacological (millimolar) rather than physiological (micromolar) concentrations. However, a concern that may arise with high-dose vitamin C treatment of pneumonia is that it produces an osmotic cell death of immune cells, rather than apoptosis, which could generate a local inflammation in the alveoli. Some authors (Gonzales, 2020) therefore recomend IV glucocorticoid treatment to attenuate the possible inflammatory complications of high-dose vitamin C treatment. Vitamin C is capable of combating all types of viruses when given in high doses, but even at a low supplemental amount, it is helpful. This is very important for those with low incomes and few treatment options. For example, in one well-controlled, randomized study, just 200 mg/day of vitamin C given to the elderly resulted in improvement in respiratory symptoms in the most severely ill, hospitalized patients; in addition, there were 80% fewer deaths in the vitamin C group (Hunt et al. 1994).

Many physicians consider high doses of Vitamin C to be so powerful as an anti-viral agent that it may be ranked as a functional immunization for a variety of influenza strains (Saul, 2005). Supplementation with high dose vitamin C appears to be able both toprevent and help treat respiratory and systemic infections. Ascorbate at sufficiently high doses can prevent viral disease and greatly speed recovery from an acute viral infection. Quercetin is a well-known flavonoid whose antiviral properties have been investigated in numerous studies. There is evidence that vitamin C and quercetin co-administration exerts a synergistic antiviral action due to overlapping antiviral and immunomodulatory properties and the capacity of ascorbate to recycle quercetin, increasing its efficacy (Colunga Biancatelli, 2020).

Vitamin D

Whilst the WHO or the RKI in Germany still do not recommend Vitamin D supplementation for prevention and treatment of Covid-19, the number of studies on its importance has been impressive (Biesalski, 2020). It is now an integral part of the protocol of the NIH and many doctor associations around the globe, where for the first time a micronutrient stands next to allopathic drugs. Initially, it was important to find out about the potential preventative affect. A recent study looked at samples from more than 190,000 Americans from all 50 states and found that those who had deficient levels of vitamin D had 54% higher COVID positivity compared with those whose levels of vitamin D in the blood were adequate (Kaufmann, 2020). This relationship stayed the same across different races, sexes and age ranges, the study states. The risk of getting coronavirus continued to decline as vitamin D levels increased. This finding is not surprising, given the established inverse relationship between risk of respiratory viral pathogens, Including influenza, and 25(OH)D levels (Gunville, 2013; Ingham, 2014; Sabetta, 2015). Vitamin D supplementation may reduce acute respiratory infections, especially in people with vitamin D deficiency (Martineau, 2017). A previous study found that each 4 ng/mL increase in circulating 25(OH)D levels was associated with a 7% decreased risk of seasonal infection, a decrement of approximately 1.75% per ng/mL (Berry, 2011). Vitamin D deficiency on admission to hospital was associated with a 3.7-fold increase in the odds of dying from COVID-19, Nearly 60%-80%(Hernandez, 2020) of patients with COVID-19 were vitamin D deficient upon hospitalization, with men in the advanced stages of COVID-19 pneumonia showing the greatest deficit (De Smet, 2020). Another study found that the life-threatening course was 20 times more frequent with low serum vitamin D than in comparison with normal vitamin D values (Alipio, 2020). In Austria 90 % of the elderly have a significant Vitamin D deficit (Steroid, 2010). The calculated COVID-19 mortality rate from 12 European countries shows a significant inverse correlation with the mean 25(OH)D plasma concentration (Laird, 2020). In a real-time meta analysis of 43 studies, vitamin D has proven effective for COVID-19. Random effects meta-analysis of the 15 treatment studies to date shows an estimated improvement of 65%. Sufficiency studies show a strong association between vitamin D sufficiency and outcomes. Meta-analysis of the 28 sufficiency studies shows an estimated improvement of 53% (VDMeta, 2020). A study found that the greatest survival rate occurred in people taking vitamin D supplements prior to COVID infection with 93.1% of these patients surviving two weeks after diagnosis. In the patients who started taking vitamin D after diagnosis, 81.2% were alive two weeks after diagnosis. However, in the group not taking vitamin D supplements, only 68.7% survived at day 14. The research is so convincing that the government in Scotland is now passing out free vitamin D supplements to anyone who is especially vulnerable to COVID's effects (Annweiler, 2020). In a new review of the medical literature, also published in November 2020, they looked at 27 studies investigating whether vitamin D deficiency was linked to COVID-19 severity in adult and elderly patients. The reviewers found that vitamin D deficiency wasn't associated with a greater chance of developing COVID-19, but the most severe cases of COVID-19 were more likely to be deficient in vitamin D compared with people who had mild cases. People with low vitamin D levels were more likely to be hospitalized from COVID-19 and to die from the disease (Pereira, 2020). The current studies should prompt all clinicians and health authorities to seriously consider vitamin D supplementation as an additional tool in the fight against COVID-19, particularly for the prevention of infection in those at high risk of both COVID-19 and hypovitaminosis D, such as the elderly (Andrea Giustina, MD, president of the European Society of Endocrinology (Medscape, 2020)).

Vitamin K

Vitamin K functions as a coenzyme during the synthesis of the biologically active form of a number of proteins involved in blood coagulation and bone metabolism (IOM, 2001). Vitamin K plays an important role in lung function because it helps to activate elastin, the protein responsible for lung tissue flexibility. The lungs must be incredibly flexible to function well. Without enough Vitamin K, elastin becomes stiff and fibrous scarring can build up in the lungs — making it more difficult to breathe and more difficult for lung tissue to exchange oxygen. Vitamin K depletion may have devastating consequences in the lungs (Noth, 2012). During a respiratory infection like Covid-19, researchers hypothesized that people with low Vitamin K status could be at increased risk for severe respiratory symptoms (Dofferhoff, 2020). Vitamin K deficiency could be a driving force in the severity of Covid symptoms and may even be a factor in who contracts Covid in the first place. Vitamin K is not a single nutrient, but the name given to a group of vitamins of similar composition. The two main groups that occur naturally are phylloquinone, or K1, and themenaquinone, or K2. Of these two forms, vitamin K2 — in particular the subset of K2 known as MK–7 — is the one we want to target. Vitamin K2 is more bioavailable, longer lasting, and provides greater benefits in the body. Aside from dietary sources, K2 can also be produced in the body by certain beneficial intestinal bacteria. This is a reason why long-term use of antibiotics can lead to Vitamin K deficiency as it kills off this good flora.

Zinc

The antiviral effects of zinc against a variety of viruses have been demonstrated during the last decades (Read, 2019). Zinc, in addition to its role as a general stimulant of antiviral immunity, is known specifically to inhibit coronavirus RNA-dependent RNA polymerase (RdRp) (Te Velthuis, 2010). Based on the ionophore properties of HCQ, it has been hypothesised that zinc may enhance the efficacy of HCQ in treating COVID- 19 patients (Derwand, 2020). In addition, zinc might inhibit the serine protease furin (Podsiadlo, 2004). Several studies demonstrated significantly lower mortality rates associated with adequate zinc levels (Berrocal, 2020; Frontera, 2020). Furin is expressed on endothelial cells, monocytes/macrophages and smooth muscle cells in human atherosclerotic plaques (Stawowy,2005), and might therefore play a critical role in the severe cardiovascular complications of COVID-19. As furin might be responsible for favouring SARS-CoV-2 spread compared with other Betacoronaviruses (Coutard, 2020; Millet, 2014) and as furin inhibition protects from certain viral-dependent infections (Shiryaev, 2007), it may be important to evaluate the potential role of zinc in inhibiting this pathway. Zinc added to HCQ and azithromycin resulted in a significantly increased number of patients being discharged, as well as a reduction in mortality or transfer to hospice (Derwand, 2020).

Selenium

Selenium is a trace element essential to human health largely because of its incorporation into selenoproteins that have a wide range of protective functions. Selenium has an ongoing history of reducing the incidence and severity of various viral infections; for example, a German study (Moghaddam, 2020) found selenium status to be significantly higher in serum samples from surviving than in non-surviving COVID-19 patients. Furthermore, a significant, positive, linear association was found between the cure rate of Chinese patients with COVID-19 and regional selenium status. Moreover, the cure rate continued to rise beyond the selenium intake required to optimise selenoproteins, suggesting that selenoproteins are probably not the whole story. Nonetheless, the significantly reduced expression of a number of selenoproteins, including those involved in controlling ER stress, along with increased expression of IL-6 in SARS-CoV-2 infected cells in culture suggests a potential link between reduced selenoprotein expression and COVID-19-associated inflammation (Zhang, 2020). The synthetic redox-active selenium compound, ebselen, has been found experimentally to be a strong inhibitor of the main SARS-CoV-2 protease that enables viral maturation within the host. That finding suggests that redox-active selenium species formed at high selenium intake might hypothetically inhibit SARS-CoV-2 proteases (Zhang, 2020). Selenium supplementation has been noted to stimulate T-cell proliferation and

enhance innate immune-system functions (Huang, 2019). Supplementation of 200 µg/day (as sodium selenite) for 8 weeks caused large increases in cytotoxic T cells and Natural Killer (NK) cells by upregulating receptors for the growth regulatory lymphokine, interleukin-2 and consequently, the rate of cell proliferation and differentiation into cytotoxic cells (Kiremidjian-Schumacher, 1994). It is well-documented that Se deficiency is associated with higher susceptibility to RNA viral infections and more severe disease outcome (Hiffler, 2020). Se might be beneficial via restoration of host antioxidant capacity, reduction of apoptosis and endothelial cell damage as well as platelet aggregation. It also appears that low Se status is a common finding in conditions considered at risk of severe COVID-19, especially in the elderly (Hiffler, 2020). Although increased blood concentrations of Se can be achieved with various pharmacological preparations, only one chemical form (sodium selenite) seems to offer true protection. Sodium selenite, but not selenate, can oxidize thiol groups in the virus protein disulfide isomerase rendering it unable to penetrate the healthy cell membrane. In this way selenite inhibits the entrance of viruses into the healthy cells and abolishes their infectivity. This simple chemical compound can therefore potentially be used in the recent battle against the coronavirus epidemic (Kieliszek, 2020).

Potassium/Calcium

COVID-19 severity is associated with lower serum concentrations of sodium, potassium and calcium. It is recommended that electrolytes be measured at initial presentation and serially monitored during hospitalization in order to establish timely and appropriate corrective actions (Lippi, 2020). It was observed that post covid patients can suffer long-term from hypokalemia and hypomagnesemia and thus this should be monitored to avoid arrhythmias and seizures (Alnafiey, 2021). Recent evidence has associated COVID-19 with hypokalemia and other ion imbalances, with potential implications for patient management, and causal mechanisms leading to hypokalemia have been proposed (Chen, 2020; Lippi, 2019; Tzcan, 2020; Moreno, 2020; Silhol, 2020; Wong, 2020). Quite interestingly, Moreno-Pérez et al. (Moreno, 2020) have described hypokalemia as a marker of disease severity and of the need for mechanical ventilation in COVID-19 patients. Potassium also softens the vascular endothelium and increases nitric oxide release (Oberleithner, 2009).

Magnesium

Constant monitoring of ionized magnesium status with subsequent repletion, when appropriate, may be an effective strategy to influence disease contraction and progression. The peer-reviewed literature supports that several aspects of magnesium nutrition warrant clinical consideration. Mechanisms include its "calcium-channel blocking" effects that lead to downstream suppression of nuclear factor-Kβ, interleukin-6, c-reactive protein, and other related endocrine disrupters, its role in regulating renal potassium loss and its ability to activate and enhance the functionality of vitamin D, among others (Wallace, 2020). It was observed that post covid patients can suffer long-term from hypokalemia and hypomagnesemia and thus this should be monitored to avoid arrhythmias and seizures (Alnafiey, 2021).

NAC

N-Acetyl-L-cysteine (NAC) is a precursor of reduced glutathione (GSH). Due to its tolerability, this pleiotropic drug has been proposed not only as a mucolytic agent, but also as a preventive/therapeutic agent in a variety of disorders involving GSH depletion and oxidative stress. At very high doses, NAC is also used as an antidote against paracetamol intoxication. Thiols block the angiotensin-converting enzyme 2 thereby hampering penetration of SARS-CoV-2 into cells. Based on a broad range of antioxidant and anti-inflammatory mechanisms, the oral administration of NAC is likely to attenuate the risk of developing COVID-19, as it was previously demonstrated for influenza and influenza-like illnesses. Moreover, high-dose intravenous NAC may be expected to play an adjuvant role in the treatment of severe COVID-19 cases and in the control of its lethal complications, also including pulmonary and cardiovascular adverse events (De Flora, 2020). NAC helps to

prevent and control RNA virus infections by amplifying functions of TLR7 and mitochondrial antiviral-signaling protein (MAVS) in evoking type 1 IFN production (Mc Carty, 2020).

Glutathione

Glutathione in its reduced form (GSH) and glutathione peroxidase (GPx) are the most essential antioxidants, both intra- and extracellular. They neutralize reactive oxygen species (ROS) and convert them to nontoxic products (H2O) (Buinitskaya, 2020). Phase 2 inductive nutraceuticals as ferulic acid and resveratrol induce various peroxidase enzymes (enzymes that neutralize hydrogen peroxidase, a ROS) and promote synthesis of glutathione. Glutathione production can also be promoted by administration of N-acetylcysteine. The utility of N-acetylcysteine in the elderly might reflect the fact that plasma cysteine levels and cellular glutathione levels tend to decline with advancing age. A common denominator in all conditions associated with COVID-19 appears to be the impaired redox homeostasis responsible for reactive oxygen species (ROS) accumulation. Levels of glutathione (GSH), the key antioxidant guardian in all tissues, could therefore be critical in extinguishing the exacerbated inflammation that triggers organ failure in COVID-19 (Silvagno, 2020). Several pieces of evidence reported in our biochemical analysis suggest that low levels of GSH could be one of the major causes of the excessive inflammatory response linked to severe COVID-19 symptoms and indicate that increasing body GSH could reduce the number of symptomatic patients (Silvagno, 2020). SARS-CoV-2 can unbalance a high activity of the renin-angiotensin system in the lung via ACE2 downregulation, followed by free radical-mediated inflammation, and unveils the protective role of GSH as an essential treatment part. It can be supplemented as the precursor NAC or in its reduced form (reduced Glutathione). A study by Khanfar et al. (Khanfar, 2020) showed that GSH depletion may have a central role in COVID-19 mortality and pathophysiology. Elevating the GSH level in tissues may therefore decrease the severity and mortality rates of COVID-19.

Quercetin

Quercetin exhibits both immunomodulatory and antimicrobial effects in preclinical studies (Aucoin, 2020). Quercetin is a polyphenolic compound, a type of flavonoid, which is found in a variety of plants consumed by humans and available as a dietary supplement. Its physiologic effects include antioxidant, anti-inflammatory, immunomodulatory and anti-pathogenic properties (Niemann, 2007; Henson, 2008; Heinz, 2010). Animal and in vitro studies have demonstrated the effects of quercetin on immune activity including increased neutrophil chemotaxis, macrophage phagocytosis, NK cell lytic activity and mitogen-stimulated lymphocyte proliferation. Quercetin regulates the expression of some genes related to cytokine production (Henson, 2008). When added to cell cultures, quercetin exerts antiviral and antibacterial properties, including inhibition of influenza A strains H1N1, H3N2 and inhibition of H5N1 entry (Wu, 2016). When looking for new antiviral compounds, knowledge of the main viral proteins is fundamental. The major druggable targets of SARS-CoV-2 include 3-chymotrypsin-like protease (3CLpro), papain-like protease (PLpro), RNA-dependent RNA polymerase, and spike (S) protein. Quercetin inhibits 3CLpro and PLpro with a docking binding energy corresponding to -6.25 and -4.62 kcal/mol, respectively. Quercetin has a theoretical, but significant, capability to interfere with SARS-CoV-2 replication, with the results of a study showing this to be the fifth best compound out of 18 candidates (Derosa, 2020). On the basis of the COVID-19 clinical manifestations, the multifaceted aspect of quercetin as both antiinflammatory and thrombin-inhibitory actions, should be taken into consideration. As mentioned above there is evidence that vitamin C and quercetin co-administration exerts a synergistic antiviral action due to overlapping antiviral and immunomodulatory properties and the capacity of ascorbate to recycle quercetin, increasing its efficacy (Colunga Biancatelli, 2020). Studies of other coronaviruses, such as SARS and MERS, suggest that quercetin has sufficient potential to treat COVID-19. Previous studies have shown that quercetin reduces the entry of the virus into the cell by blocking the ACE2 receptor, as well as reducing the level of interleukin-6 in SARS and MERS patients (Bastaminejad, 2020).

Quercetin and Zinc

Zinc is a decidedly anti-viral mineral. High intracellular concentrations inhibit the replication of RNA type viruses, such as SARS-CoV-2. Zinc does this by blocking RNA-dependent RNA polymerase (RdRp), the core enzyme of their multiprotein replication and transcription complex that is critical for the copying of viral RNA. That's the conundrum. In high concentrations, zinc can block coronavirus reproduction, but the cell is typically disinclined to tolerate high levels of zinc due to concerns about its other actions. Enter the zinc ionophores. Fortunately, there are molecules that can act as facilitators and enhance the entry of zinc into the cell. These, e.g. chloroquine, are known as zinc ionophores, and here's the payoff: in addition to its effects on endosome pH, chloroquine has been shown to be a zinc ionophore, but there's even more to the story. In addition to chloroquine, the nutraceuticals quercetin (bioflavonoid) and epigallocatechin-gallate (green tea polyphenol) are also zinc ionophores (Dabbagh-Bazarbachi, 2014). Quercetin plus zinc is being tested as an antiviral in human clinical trials for the treatment of Covid-19 . The combination had already made it through animal trials for use against Ebola and SARS-CoV1, and was approved by the FDA for human clinical trials. Plans are underway for a large-scale trial in China for patients with Covid-19. Foods that have a high ratio of lysine over arginine such as eggs, tofu, fish (not raw), sardines, have been shown to block replication of all coronaviruses including COVID-19.

Lysine

Lysine therapy interrupts the replication of viruses, including COVID-19 coronavirus, by countering arginine, an amino acid that fosters the eruption of dormant viruses. Lysine has been safely used for decades to quell herpes virus outbreaks that cause cold sores on the lips (herpes labialis), a treatment pioneered by one of the Bio-Virus Research team members in 1974. Lysine is available in foods and in concentrated form in inexpensive dietary supplements (250 500-milligram lysine tablets). Lysine/arginine imbalance would explain why patients who have been infected with COVID-19 have recurrent infections, even after vaccination. IL-10 inhibits the synthesis of IL-6, TNF and IL-1 beta, which are implicated in fever. IL-10 serves as an endogenous antipyretic. Lysine deficiency raises IL-6 inflammatory cytokine levels, so lysine potentially has an IL-6 inhibitory effect, and lysine also increases IL-10 anti-inflammatory cytokines as shown in the liver. It is therefore logical to assume that supplementation with lysine could restore or augment IL-10 levels resulting in downregulating proinflammatory cytokines, in turn eliminating fevers and cytokine storms. IL-6 inhibitors for patients with severe Covid-19 are associated with decreased intubation, reduced mortality, and increased discharge. L-lysine decreases nitric oxide production, thereby limiting a key role in the pathogenesis of inflammation, and thus lysine may serve an anti-inflammatory role by reducing pro-inflammatory cytokines (Lysine Therapy for SARS-CoV-2, Chaihorsky, A.: https://www.researchgate.net/publication/344210822).

pH lowering agents

The increasing evidence suggests that the entry, replication and infection processes of several viruses such as Ebola, Marburg, dengue, Chikungunya, HIV etc. are highly dependent on endosomal-lysosomal acidification and the activities of several host endosomal proteases - which are also active in acidic pH environments (Sun, 2012; Barrow, 2013). The influenza virus entry is mediated by the acidic-pH-induced activation of hemagglutinin (HA) protein (Zaraket, 2013). Chloroquine analogs for example, by neutralizing the acidic pH in endosomes, inhibit these viral entry and replication processes into the cytoplasm of susceptible cells and thereby abrogate their infections (Chiang, 1996; Savarino, 2003). The antiviral action of the analogs has been shown to inhibit acidification of the endosomes during events of replication and infection (Al-Bari, 2017). The antiviral effects of Chloriquine shown against Zika, Chikungunya, and HIV are due to the cancellation of endosomal/lysosomal acidification. Recently, CQ and HCQ were approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients infected with the coronavirus SARSCoV- 2, causing the disease which originated in December 2019, namely COVID-2019 (Martinez, 2020). In a study by Henson (Henson, 2020) the infectivity of VN-H5N1 increased about 3.5-fold at pH 7.0 compared with that at pH 7.7

and then gradually decreased at pH 6.5, 6, and 5.5. In marked contrast to the infectivity of VN-H5N1, the infectivity of K582I was very low at pH 7.7, and it was enhanced by 2 orders of magnitude when the pH of the infection medium was lowered to 7.0. Furthermore, whereas the infectivity of VN-H5N1 reached its maximum at pH 7.0, the peak of infectivity of K582I was shifted to pH 6.0 to 6.5. This could stress the importance of plant-based nutrition in viral disease, i.e. maintaining a high pH.

Spirulina

Spirulina, a filamentous cyanobacterium, possesses diverse biological activities and nutritional significance due to its high concentration of natural nutrients, having bio-modulatory and immuno-modulatory functions. Different Spirulina preparations influence the immune system, viz. they increase the phagocytic activity of macrophages, stimulating the production of antibodies and cytokines, they increase the accumulation of NK cells into tissues as well as the activation and mobilization of T and B cells. Spirulina have also been shown to perform a regulatory role on lipid and carbohydrate metabolism by exhibiting glucose- and lipid-profile correcting activity in experimental animals and in diabetic patients. Preparations have been found to be active against several enveloped viruses including herpes virus, cytomegalovirus, influenza virus and HIV (Khan, 2005). Spirulina possesses a direct effect on both innate (activation of macrophage and NK cells) and specific immunity (regulation of T cells and increased production of antibodies) (Cicero, 2018; ; Khan, 2005; Hirakashi, 2002). Its antiviral properties even against influenza and herpes virus (Hernández-Corona, 2002) have been known for years (Abd El-Baky, 2020; Chen, 2016). Anti-flu efficacy studies revealed that the Spirulina extract inhibited viral plaque formation in a broad range of influenza viruses, including oseltamivir-resistant strains. Spirulina extract was found to act at an early stage of infection to reduce virus yields in cells and improve survival in influenza-infected mice, with inhibition of influenza hemagglutination identified as one of the mechanisms involved (Chen, 2016). Phycocyanobilins present in spirulina may have potential for boosting type 1 IFN response in the context of RNA virus infection (Mc Carty, 2020). The ability of algae-based nutraceuticals, mainly Spirulina, to boost immunity against viral diseases has already been reported clinically. Spirulina-based nutraceuticals boost the adaptive and innate immunity, and bioactive compounds, such as angiotensin-converting enzyme (ACE) inhibitor peptides, phycobiliproteins, sulfated polysaccharides, and calcium-Spirulan, which can serve as antiviral agents. The presence of these molecules indicates its potential role in resisting infection and COVID-19 disease progression (Ratha, 2021).

Artemesia annua

For millennia, herbal folk medicines in Asia, Africa, and South America have been used to treat infectious diseases. Extracts of A. annua plants have been successfully employed to treat febrile diseases including malaria. Artemisinin is extracted from this plant and is the basis for the WHO-recommended anti-malaria combination therapies used in millions of adults and children each year with few, if any, side effects. A. annua has shown significant activity against several viruses (Kim, 2015) and SARS coronavirus that occurred in 2002 (Haq, 2020). In 2003, Li et al. (Li, 2003) had indicated that artemisinin is one of the candidates for treating severe acute respiratory syndrome coronavirus (SARS-CoV) (Jo, 2020). A. annua extracts worked significantly better than pure artemisinin derivatives and the addition of coffee further enhanced the activity (Gilmore, 2020). A trial with extracts of the plant A. annua which are active against SARS-CoV-2 is currently being carried out by a cooperation between scientists from the Max Planck Institute, University of Kentucky and Freie Universität Berlin. Trials have already demonstrated that extracts of the medicinal plant, Artemisia annua L., which produces the antimalarial drug artemisinin, prevent SARS-CoV-2 replication in vitro (Nair, 2021). Algerian researchers had tested the effectiveness of malaria drugs against SARS-CoV-2 in April. Their study proved that artemisinin was more effective than hydroxychloroquine. Artemisia annua has recognized antiviral activity (anti HSV1, Poliovirus, RSV, hepatitis C anti-virus, type 2 dengue virus, hantavirus, human cytomegalovirus) and anti-HIV activity in vitro thanks to the flavonoids, quercetin and dicaffeoylquinic acids it contains. These molecules have been shown to inhibit the enzymatic activity of CLPro (Chymotrypsin-like protease), an enzyme produced by SARS-CoV-2 (Benatouil, 2020). The antiviral action of Artemisia annua,

which is achieved by stimulating adaptive immunity, regulating the production of the pro-inflammatory cytokines prostaglandin E2 (PGE2), IL-6, IL-10 and TNF alpha, and increasing the genesis of CD4, CD8 and interferon gamma, involves many minerals and biomolecules: the properties of flavonoids, polyphenols, triterpenes, sterols, saponins, polysaccharides, artemisinin and its derivatives, the concentration of zinc, gallium and selenium in the plant play a role in its immune, antiviral, antioxidant and anti-inflammatory response. The plant is rich in Vitamins A and E, of which one, when supplemented, is known to reduce morbidity and mortality in viral infections, HIV among others, and the other is a powerful antioxidant. At the end of April, Madagascar's President Andry Rajoelina touted a potion containing an Artemisia extract and other herbs as a "miracle cure" for the coronavirus. Since then, media in Africa have plugged the drink's potential, and several African countries have placed orders for the herbal tonic, sold under the name COVID Organics (DW, 2020). While some African countries, such as Tanzania, Togo and Chad have reportedly ordered the potion, others – like Nigeria – are being more cautious. While it's possible new treatments might come from traditional medicines, says Michel Yao from the WHO Regional Office for Africa, people should refrain from using untested remedies for coronavirus. At the time of the writing of this paper (January, 2021) the Covid death rate was 281, with 19,065 cases reported (WO, 2020).

Glycyrrhizin (Liquorice root)

Glycyrrhizin (GZ) has been the topic for the creation of new antiviral drugs based on glycyrrhizic acid and its derivatives for years (Baltina, 2020) and is a promising agent against SARS-CoV-2 as its antiviral activity against SARS-CoV has already been confirmed. It is worthwhile to extrapolate from its proven therapeutic effect as there is a high similarity in the structure and genome of SARS-CoV and SARS-CoV-2. There are many possible mechanisms through which GZ acts against viruses: increasing nitrous oxide production in macrophages, affecting transcription factors and cellular signalling pathways, directly altering the viral lipid-bilayer membrane, and binding to the ACE2 receptor (Chrzanowski, 2020). It exhibited anti-inflammatory potential by decreasing the production of prostaglandin E2, TNF-alpha, and intracellular reactive oxygen species (ROS), and reducing the expression of cyclooxygenase-2. Moreover, it exhibited anti-allergic activity through decreased levels of IL-4 and thus restored the proper TH1/TH2 cell ratio, resulting in the inhibition of antigen-specific IgE production by B cells (Han, 2017). Several studies have revealed the antiviral activity of GZ against viruses of the Flaviviridae family, and HIV, HBV, HCV, HPV, and influenza virus (Crance, 2003; Ikeda, 2006; Sasaki, 2003; van Rossum, 1998; Wang, 2015). In one study computational approaches were employed, especially structure-based virtual screening followed by molecular dynamics (MD) simulation as well as binding energy analysis for the computational identification of specific terpenes from the medicinal plants, which can block SARS-CoV-2 S-RBD binding to human angiotensin-converting enzyme 2 (H-ACE2) and can act as potent anti-COVID-19 drugs after further advancements. The screening of focused terpene inhibitors database composed of ~1000 compounds with reported therapeutic potential resulted in the identification of three candidate compounds, NPACT01552, NPACT01557 and NPACT00631 (Glycyrrhizin). All these compounds showed stable conformation and interacted well with the hot-spot residues of SARS-CoV-2 S-RBD (Muhseen, 2020). Glycyrrhizin may reduce the severity of an infection with COVID-19 at the two stages of the COVID-19 induced disease process: 1. To block the number of entry points and 2. To provide an ACE2 independent anti-inflammatory mechanism (Murck, 2020). Glycyrrhizic acid also inhibits TLR agonists induced IL-6 production in macrophage (Yang, 2020). It has been used against inluenza viruses for decades in China. Its multiple effects in the Covid pathophysiology should make it an integral part of a Covid protocol.

Chinese Herbs

Traditional Chinese Medicine (TCM) has played an important role in the prevention and control of the epidemic in China (Jiao, 2020). Chinese herbal medicine is widely used in combination with conventional medical care there (Xia, 2020). It is said that the low mortality rate of Covid in China is based on using TCM herbs in the treatment protocols (Rausch, 2021). In recent years, Shufeng Jiedu (SJ) has been used in China to treat diseases such as influenza, upper respiratory tract infections, chronic bronchitis, and community-

acquired (Liu, 2020)). Screening of the herb mixture resulted in 163 compounds and 463 targeted genes (Xiong, 2020). SJ has since been studied alone or in combination with other treatment modalities. Through network pharmacology analysis, SFJDC was found to effectively improve immune function and reduce inflammatory responses based on its key compounds, hub target genes, and the relevant pathways. These findings may provide valuable evidence for explaining how SFJDC exerts therapeutic effects on COVID-19, providing a holistic view for further clinical application (Zhuang, 2020). One study of a treatment regimen of Shufeng Jiedu capsules combined with Arbidol to treat common-type Covid-19, combining traditional Chinese and western allopathic medicine, improved time to recovery, had better clinical effectiveness, and was considered safe (Chen, 2020). SFJDC significantly reduced the virus load in the lungs of HCoV-229E mice (from 1109.29 ± 696.75 to 0 ± 0 copies/ml), decreased inflammatory factors IL-6, IL-10, TNF-α, and IFN-γ in the lung, and increased the amount of CD4+ and CD8+ cells in the blood compared with the model group (Xia, 2020). The properties of the top 10 Chinese herbs included antiviral, antibacterial, anti-inflammatory, antipyretic and analgesic, anti-acute lung injury, anti-shock, immune regulation, and enhancement of pulmonary function. In addition, clinical research results and Chinese treatment data showed that the CPMs had good therapeutic efficacy in the treatment of COVID-19, and adverse reactions were minimal (Zhuang, 2020). In a drug combination mainly including a Ganlu Xiaodu decoction, Abidor, Lianhua Qingwen, Moxifloxacin, Qiangli Pipa Lu, vitamin C, glycyrrhizinate diammonium, pantoprazole and Shufeng Jiedu: of 131 Covid cases, all patients were released from hospital symptom-free (Chen, 2020). Studies are suggesting that SFJDC alone or in combination might be a promising drug for the treatment of Covid-19 (Xia, 2020; Wang, 2020; Tao, 2020; Chen, 2020; Li, 2020, Xiong, 2020, Ma, 2020; Yang, 2020).

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HBOT

HBOT (Hyperbaric Oxygen Therapy) is the use of concentrated oxygen. There are numerous studies out proving the high efficiency in Covid-19 disease. Ventilators at sea level are increasing the gas pressure at the alveoli by about 1%-2% and in doing so risk pneumothorax and require extensive clinical skill sets. 1000 cm H20 is the ambient pressure in NYC ICUs and then the little endotracheal tube adds 10 cm H2O additional pressure for a total gas pressure of 1010 cm H2O. A hyperbaric chamber at 1.5ATA increases gas pressure by 50% and at 2ATA, the increase is 100%. At 1.5ATA we are looking at 1500cmH20 gas pressure and at 2ATA 2000cmH20.

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https://pubmed.ncbi.nlm.nih.gov/32931666/
https://pubmed.ncbi.nlm.nih.gov/32541128/

Professor Philip James of the University of Dundee in Scotland originally proposed the concept of re-purposing the Concordes as large hyperbaric Chambers. I n early April of 2020 a USAF cargo jet landed at RamsteinAFB/Landstuhl.
https://www.airforcetimes.com/news/your-air-force/2020/07/05/first-aeromedical-evacuation-conducted-with-new-containment-chamber-for-covid-19-patients/
AircraftHBOT.org
Air compressors to do this:
https://skygeek.com/tronair-15b7603-1000-cabin-pressure-unit-230vac-60.html
https://www.tronair.com/products/Air-Conditioning-and-Cabin-Pressure-Testing-ATA-21/Cabin-Pressure/Cabin-Pressure-Test-Unit-Portable
Swiss company:
https://www.stssensors.com/blog/2020/07/01/cabin-pressure-testing/

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