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# *Integrative and proactive strategies for maintaining health in the era of COVID-19*

## PART 1- BREATHING AND MIND-BODY THERAPIES

### Introduction

The global pandemic of COVID-19, caused by a new variety of coronavirus called SARS-CoV-2, is a respiratory illness that in some people causes severe lung pathology which can lead to respiratory failure and sepsis. The current mortality rate is reported to range from 3-9% [1]. The SARS-CoV-2 virus is particularly dangerous because there is no existing immunity in humans. The virus spreads quickly and easily from person to person from droplets in the air, on surfaces and from faeces and urine. Hygiene measures such as hand washing, cleaning of surfaces and social distancing are essential measures to control exponential growth of the spread of this virus through our global community.

The early symptoms of COVID-19, which can include fever, coughing, sore throat, myalgia, malaise, headache, diarrhoea and shortness of breath are relatively mild for the majority of people. In others the infection can progress quickly to a pneumonia that can be fatal in older individuals and in those with pre-existing medical conditions. However, there have been fatalities recorded in young individuals with no known pre-existing conditions.

People who become severely ill after infection with SARS-CoV-2 virus do so due to a maladjusted immune response, with overwhelming and destructive inflammatory processes damaging the lungs and other organs [2]. In the severe pulmonary manifestations of this disease massive inflammatory cell infiltration and elevated pro-inflammatory cytokine/chemokine responses can lead to acute lung injury (ALI), and acute respiratory distress syndrome (ARDS)[3]. Patients with mild COVID-19 symptoms can suddenly progress to severe disease due to viral activation of the cytoplasmic NLRP3 inflammasome within macrophages and Th1 immune cells. Once activated, the inflammasome releases proinflammatory cytokines such as IL-1 $\beta$ , IL-6, TNF- $\alpha$  and other inflammatory factors like chemokines and high mobility group box protein (HMGB1) that respond in a cascade sometimes referred to as a cytokine storm[4]. Recent research has also shown that lung damage can begin in asymptomatic patients during early stages of the COVID-19 infection[5].

While there are no clinically proven evidence-based integrative prevention or treatment strategies for COVID-19 infection, proactive strategies that support general immune function and reduce inflammation seem prudent but cannot be guaranteed to provide

any specific outcome in regards to COVID-19. World health organisations, as well as state and federal health and consumer agencies throughout the world, are warning the public not to fall for fake remedies, and health practitioners are rightly being warned not to provide false and misleading advertising on COVID-19. With these cautions in mind this article offers an exploration of some of the research on how self-care strategies such as proper breathing, healthy diet, sleep, stress reduction, nutritional supplementation and traditional herbal medicines might affect the body's response to the virus. It also looks at how these factors might influence pathological processes occurring in COVID-19.

### Can nasal breathing and nitric oxide be protective?

Our nose is one of our primary lines of defence against airborne pathogens. It also protects the lungs by filtering, warming and moistening inhaled air.

Breathing through the nose significantly reduces particle deposition in the lungs that occurs during mouth breathing [6]. The nose has a very sophisticated system for protecting the whole airway from infection and one of the key mechanisms involves the production of nitric oxide (NO) within the nose and nasopharynx [7, 8].

NO provides immune protection by its upregulation of ciliary motility and through direct antiviral and antimicrobial activity of nasally derived NO [9]. NO also improves pulmonary function and oxygenation through its effects on the pulmonary circulation, with research showing that nasal breathing increases blood oxygen levels by around 10% [10].

Research conducted during a previous Coronavirus epidemic, the SARSCoV (Severe Acute Respiratory Syndrome Coronavirus) epidemic, showed that NO inhibited the replication of SARSCoV in a dose-dependent manner, meaning that higher levels had a greater inhibitory effect on the replication of the virus [11]. Another trial showed that NO reversed pulmonary hypertension, improved severe hypoxia and shortened the length of ventilatory support as compared to matched control patients with SARS-CoV [12].

Several clinical trials are currently under way using NO inhalation for prevention and treatment of COVID-19. In one study health workers are being asked to spend 20 minutes twice per day breathing in a gas mixture with high concentrations of NO to see if this reduces their incidence of infection [13]. Other randomised controlled trials are investigating whether the inhalation of NO in addition to standard therapy improves oxygenation and increases survival in hospitalised patients with moderate and severe lung complications from COVID-19 [14].

Nasal breathing and breathing techniques such as humming and particular types of controlled breath-holding stimulate increased NO production. Because the nasal airways and sinuses are the primary sources of exhaled NO, nasal breathing concentrates the amount of NO circulating in the upper airway [15]. Levels of NO are reduced by 50% if we switch to mouth breathing [16]. Nasal breathing also makes the nose healthy in other ways, improving its microbiome, hydration, blood flow and mucus

production [17][8]. Humming is able to increase NO levels 15-fold as compared to normal quiet breathing. Research has shown that after humming nasal NO output increased from 189 nl/minute (17 parts per billion) to 2818 nl/minute (252 parts per billion) [18].

Humming has been applied therapeutically for the treatment of chronic sinusitis [19, 20] [12, 13]. A case study of a patient who had been unable to nose breathe due to chronic sinusitis for a month showed that he was able to achieve a clear nose and breathe easily through his nose after 4 days of intensive humming (one hour the first day and 120 hums 4x per day thereafter). The authors hypothesised that the effect was due to the increase in NO produced by the humming [21].

Breath-holding can also help reduce blocked noses and has been shown to increase NO [22]. The concentration of NO in the nasal passages and the nasopharynx increases after breath-holding with voluntary closure of the soft palate [16]. In cases of nasal obstruction, breath-holding after exhalation for up to 30 seconds can reduce nasal resistance, and the effect lasts over time [23].

### Breathing and mind-body techniques for stress, immunity and inflammation

Psychological stress can downregulate the cellular immune response and disrupt the complex homeostatic networks that maintain the health of the immune system. The consequences of this include increased susceptibility to viral infections [24, 25].

Psychological stress also increases inflammation, with evidence of a bi-directional relationship between these two factors. Stress initiates release of cytokines such as IL-1 $\beta$  and TNF $\alpha$  IL which in turn can cause activation of the inflammasome [26]. Once the inflammasome is activated there can be adverse changes in neurotransmitters, with reduced serotonin levels. Subsequent anxiety and depression

maintain the stress response and the increased inflammation [27].

### Breathing and mind-body practices

Breathing and mind-body practices can reduce stress and influence immune and inflammatory states. There has been extensive research, and a recent systematic review of 26 randomised controlled trials of a diverse range of mind-body therapies showed changes in genomic markers, with decreased expression of inflammation-related genes [28]. Another meta-analysis showed that mind-body therapies reduced circulatory and cellular markers of inflammation and influenced virus-specific immune response [29].

Mindfulness meditation, one of the most widely accepted and researched forms of mind-body practices in recent times, has been shown to improve immune function and reduce inflammation markers. Some of the effects of mindfulness meditation include changes in inflammation markers and increased cell-mediated immunity [30]. Mindfulness meditation reduces IL-6 and effects persist with ongoing practice [31]. The effects are strongest in susceptible individuals with pre-existing inflammation [32]. However mindfulness meditation is not always easy for individuals who are under a large amount of stress or who suffer from the effects of trauma, anxiety or depression. Mind-body practices that include specific breathing and movement practices can be easier to comply with for some of these people.

Conscious modulation of breathing according to various traditional and modern methods that link both dynamic and relaxed breathing practices with mental focus, body postures and movement has been shown to support immune system homeostasis. Increased natural killer cell activity and increased immune-related gene expression have been observed in immune-compromised individuals and in healthy individuals practising Sudarshan Kriya, a breathing sequence derived from pranayama [33, 34]. Qigong, Tai

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Chi and the Japanese Nishino practice have all been demonstrated to provide both immediate and long term support and regulation to the immune system, increasing natural killer cells as well as lymphocyte and monocyte numbers and reducing pro-inflammatory cytokines [35-37]. The potential potency of breathing modulation is highlighted in one randomised controlled study where a group of healthy subjects trained for 10 days in Wim Hof method were able to withstand injection with bacterial endotoxin, demonstrating greatly reduced flu-like symptoms and much lower levels of pro-inflammatory cytokines (e.g. TNF-alpha, IL-6, and IL-8) than the control group [38].

### **Sleep and related breathing disorders**

Sleep is a well-known modulator of natural immunity. A single night of partial sleep deprivation was shown to reduce natural killer cell activity to 72% of its normal function [39]. The pro-inflammatory effects of sleep deprivation are also well known. Reductions by 25% and 50% of a normative 8 hours of sleep led to shifts in basal inflammatory cytokines in even healthy, asymptomatic individuals [40].

The epidemic of sleep disordered breathing (SDB) has important implications for sleep, stress, inflammation and immunity. Severe forms of SDB such as obstructive sleep apnoea, and less obvious forms such as upper airways resistance syndrome, are important causes of sleep disruption, insomnia [41, 42], autonomic dysregulation [43], chronic stress and systemic inflammation [44, 45].

### **Breathing techniques for lung function, oxygen and breathlessness**

A plethora of breathing techniques has been promoted via social media and in the popular press for managing breathlessness and assisting with COVID 19 lung symptoms and pneumonia. In hospitals respiratory physiotherapists use various means, such as PEPE airway clearance devices and

breathing techniques, as active cycle of breathing techniques (ACBT) to clear mucus from the lungs in patients with pneumonia. However, these are only used in about 35% of patients who have productive cough and are considered counterproductive in patients with dry cough [46]. Mucus production, if not excessive to the point of blocking airways, is helpful as part of the body's immune response against the virus. Patients with dry coughs generally need to reduce overly vigorous deep breathing or forced coughing to avoid irritating their airways and exhausting their energy reserves. It's also been shown that infected patients spread large amounts of mucus droplets and viral particles when they cough [47].

Forced deep breathing can lead to hyperventilation and hyperinflation of the lungs. These aggravate breathlessness and reduce the efficiency of breathing. Hyperventilation increases the reactivity of the airways, making them more prone to bronchospasm. It also reduces the oxygen available to cells by causing vasospasm and inhibiting oxygen desaturation from haemoglobin [48]. Hyperinflation, or breath stacking, is a common cause of unexplained breathlessness in patients with respiratory disease. In hyperinflation shortened, tense and functionally weak respiratory muscles are less able to respond appropriately to central motor command from respiratory centres, potentially contributing to a disparity between ventilation commanded and ventilation achieved. This type of disparity, sometimes called afferent refferent dissociation or neuromechanical uncoupling, is thought to be a key factor in determining the extent and quality of dyspnoea in patients with pulmonary disease [45, 49].

Patients managing their condition at home can be safely advised to maintain nasal breathing as much as possible and to practise relaxed, slow and slightly deeper breathing. As mentioned earlier in this article, nasal breathing protects the lungs and improves oxygen delivery. Relaxed, slow breathing also improves oxygen delivery and lung function, and helps to reduce inflammation [50-52].

## **PART 2- HERBS, NUTRITION AND SUPPLEMENTS**

### **Herbal medicines for immune defence and the inflammatory processes**

Herbal medicines have shown the potential to assist in the treatment of several types of viral infection resistant to medical treatment [53].

Different viruses use a range of strategies to enter host cells. The SARS-CoV-2 virus enters by attaching to angiotensin-converting enzyme-2 (ACE-2) linkages on the surface of cells in the respiratory tract. Some traditional herbal medicines have been demonstrated to inhibit the ability of coronaviruses to attach to ACE-2. Yang et al, in a review of research on traditional Chinese Herbal treatment of SARS-CoV-2, list Rheum officinale, Polygonum, Scutellaria baicalensis, Bupleurum chinense, Licorice (Glycyrrhiza uralensis) and Quercetin as substances which have potential to block viral entry, penetration and absorption [54]. Stephen Buhner in his book *Herbal Antivirals* mentions many of these herbs, as well as Horse Chestnut (Aesculus hippocastrum), Polygonum spp (Knotweed), Luteolin, Elderberry (Sambucus nigra) and Cinnamon (Cinnamomum cassia) as herbs that can interfere with viral attachment to ACE-2 linkages [55].

During the 2003 SARS outbreak Chinese research showed that a combination of two commonly available patent formulas, Sang Ju Yin (Mulberry Leaf and Chrysanthemum) and Yu Ping Feng San (Jade Screen Formula), appeared to dramatically reduce the rate of infection in a high-risk population of hospital workers and medical technicians. The 1063 people taking the formula were reported to have zero rate of infection as compared to a 0.4% rate of infection in the control group [56].

Some other herbs that have demonstrated anti-viral effects against other viruses but not specifically against coronaviruses include Astragalus membranaceus [57], a range of mycelial mushrooms including Cordyceps (*Cordyceps militaris*), Reishi (*Ganoderma lucidum*), Chaga (*Inonotus obliquus*), Shitake (*Lentinula edodes*), Turkey Tail (*Trametes versicolor*) [58], peppermint (*Mentha piperita*) [59], and *Andrographis paniculata* [60].

Research conducted during the COVID 19 epidemic has found that a number of traditional formulas seemed to decrease symptoms and promote recovery. In February 2020, the Chinese government issued an announcement that Chinese herbal medicine should be recommended to all COVID-19 patients. During the height of the epidemic around 85% of people in China were treated with a combination of traditional Chinese herbal medicine and antiviral, anti-inflammatory and antibiotic pharmaceuticals [54].

Herbal formulae used in China varied according to province. One of the most popular pre-made formulae, Lianhua Qingwen, showed promising results. A systematic review of this formula concluded that in capsule

form it appeared to be more effective and safer than Oseltamivir, Ribavirin and AnkaHuangmin capsules (Niu et al., 2017). Lianhua Qingwen was the first new drug variety approved by China's National Drug Administration's rapid drug approval channel during the 2003 SARS epidemic. Two studies that retrospectively analysed the clinical efficacy of this formula in confirmed and suspected COVID-19 patients concluded that it markedly relieved symptoms, and promoted recovery in patients with pneumonia [61, 62]. One hundred thousand boxes of this formula were shipped to Italy as part of the Chinese assistance to Italy during the difficult time of the Coronavirus pandemic there. [63]

Researchers investigating traditional Chinese herbal medicine identified their ability to inhibit a number of inflammatory cytokines, such as IFN- $\gamma$ , IL-1 $\beta$ , IL-6, TNF- $\alpha$ , chemokines MIP-1 $\alpha$ , MIP-1 $\beta$ , MCP-1 and other inflammatory factors such as CCL2/MCP-1 and CXCL-10/IP-10, activated during cytokine storms (common complications of respiratory diseases caused by coronaviruses) [54].

Many of the Chinese herbs used in Traditional Chinese Medicine (TCM) formulae were found to be able to inhibit inflammatory cytokines and chemokines. However, the best practice of TCM involves individualised prescription with the choice of herbs mostly dependent on the patient's stage of disease and TCM diagnostic syndrome presentation. A common remedy may be given in the prevention phase. However, in the influenza, pneumonia or recovery phases patients are categorised according to various TCM syndromes, for example, Wind Cold Invading the Exterior or Toxic Heat

Attacking the Lungs in the Influenza phase, and Shao Yang Syndrome with Damp or Damp Heat Afflicting the Lung in the Pneumonia Phase. Herbs are prescribed according to the syndrome on the basis of tongue, pulse, symptoms and physical appearance of the patient.

### Diet and nutritional supplements

Overly strict dietary regimes with limited varieties of foods, as well as highly processed diets, can be problematic for the immune system. Numerous macro- and micro-nutrient dietary deficiencies and dietary imbalances will compromise the immune system. Fibre in the diet acts as a prebiotic that supports the complex and diverse microflora needed for immune regulation. Diets high in refined starches, sugar, saturated and trans-fatty acids, poor in omega 3 fats, natural antioxidants and fibre from fruits, vegetables or whole grains can compromise the immune system and contribute to excessive production of inflammatory cytokines and reduced production of anti-inflammatory cytokines. Diets low in protein will also reduce immunity.

The Mediterranean diet is a diet that supplies good levels of micronutrients with a balance of macronutrients. It's been studied extensively for its ability to protect against a range of chronic diseases characterised by some degree of chronic inflammation. This diet has both antioxidant and anti-inflammatory properties, with a normalising effect on cytokines and other inflammatory biomarkers [64].

The Mediterranean diet is characterised by abundant consumption of olive oil, high consumption of plant foods (fruits, vegetables, pulses, cereals, nuts and seeds); frequent and moderate intake

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of wine (mainly with meals); moderate consumption of fish, seafood, yogurt, cheese, poultry and eggs; and low consumption of red meat, processed meat products and seeds. The diet includes an abundance of plant foods high in flavonoids and polyphenols, many of which have been found to reduce NLRP3 inflammasome activation of NFκB, TNF-α, IL-6, IL-1β and IL-18 expression [65].

Some specific foods from the Mediterranean diet that reduce inflammatory biomarkers and regulate cytokine secretion include olive oil, nuts [66, 67] and garlic [68]. Many other fruits and vegetables also have been shown to contain flavonoids that reduce inflammatory cytokines, including tomatoes, onion, parsley, celery, apples, oranges, berries and turmeric. Ten servings a day of these foods, rather than the usual recommendation of five, might boost the anti-inflammatory effects of plant foods in the diet.

### The gut microbiome

The composition of the gut microbiome and the integrity of the gut barrier have important implications for inflammation and immune system health. In the presence of intestinal permeability, pathogenic bacteria and inflammatory compounds are able to cross into the bloodstream. Lipopolysaccharide (LPS) found within the cell walls of many Gram-negative bacteria is one of these inflammatory compounds. LPS is released when those bacteria die. This stimulates an inflammatory cascade and immune response [69]. A healthy gut microbiome helps in the competitive inhibition of pathogenic bacteria, and it's possible that this has beneficial effects on immune resistance to viral infection.

### Fasting and immunity

Both prolonged and intermittent fasting have been shown to reduce inflammation and improve immune regulation in specific circumstances [70]. Autoimmunity and immunosenescence associated with the ageing process can be improved with certain types of modified fasting [71].

Fasting may need to be applied with some caution in the case of COVID-19, given the different effects of fasting in viral as compared to bacterial sepsis. These two types of infection have opposing metabolic requirements and cellular stress adaptations. In bacterial sepsis fasting is protective. However, it is potentially problematic in viral sepsis. The effects are independent of pathogen load and magnitude of inflammation [72].

### Dietary supplements

The complex integrated immune system needs adequate quantities of multiple micronutrients working synergistically at the various stages of the immune response. Vitamins A, D, C, E, B6, B12, and folate, zinc and iron all play a role in immunity. Micronutrients with the strongest evidence for immune support are vitamins C and D and zinc [73].

### Zinc

Zinc has long been known to improve resistance to viral infection. There is research showing zinc causes increased cellular resistance to the SARS CoV and reduces its virulence [74, 75].

### Vitamin D

Low vitamin D levels are associated with an increased incidence of upper respiratory tract infections and chronic lung inflammation [76, 77]. Vitamin D is a direct and indirect regulator of T cells and its effects are particularly useful for prevention of viral infection [78]. Vitamin D can also help to inhibit inflammasome activation pathways and reduce inflammatory cytokines in certain chronic illness [79, 80]. It has been recommended that blood levels of vitamin D be kept above 40-60 ng/mL (100-150 nmol/L) to mitigate the severity of COVID-19 [81].

### Vitamin C

A large number of research trials have explored the use of vitamin C for preventing and treating respiratory infections ranging from the common cold to pneumonia, and though it appears that routine mega-doses of Vitamin C

for prevention of the common cold are not justified [82], one systematic review identified several randomised controlled trials showing an 80% to 100% reduction in the incidence of pneumonia in participants taking vitamin C as compared to controls [83]. Ascorbic acid in conjunction with quercetin inhibits NLRP3 inflammasome activation [84].

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# ElementAll™ Diet

## Nutritionally Complete Hypoallergenic Formula

ElementAll™ Diet is a nutritionally complete formula to aid repair of the gastrointestinal wall lining and support small intestinal health. Containing pure, 100% free-form amino acids, readily absorbed carbohydrates and MCT, this hypoallergenic formula contains the daily recommended allowances for all nutrients, vitamins and minerals in easily digestible forms.

By delivering nutrients in easily digestible forms, ElementAll™ Diet relieves digestive discomfort. Free-form amino acids are absorbed into the bloodstream from the proximal part of the small intestine and allows for an almost immediate assimilation. The result being a significant reduction in the reaction of food particles within the digestive tract and a decrease in inflammatory symptoms associated with various gastrointestinal conditions.

