6 STEPS TO OPTIMISING YOUR IMMUNE HEALTH

"Health is a state of complete mental, social and physical well-being, not merely the absence of disease or infirmity."

- World Health Organization

1948

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INTRODUCTION

There is widespread evidence available for interventions that support immunity, protect against viral infection and may possess antiviral activity. This leaflet covers the main dietary and lifestyle components that, when optimised, can help improve immune status and resistance to infections. The recent COVID-19 pandemic has made all of us keen to help our immune system "be the best it can" as it is our first and best level of protection from COVID-19 and other viral infections.

The recent lockdown has also created many challenges for people who were suddenly unable to follow their normal health routine and whose stress levels have been increased by this and other impacting factors of the pandemic.

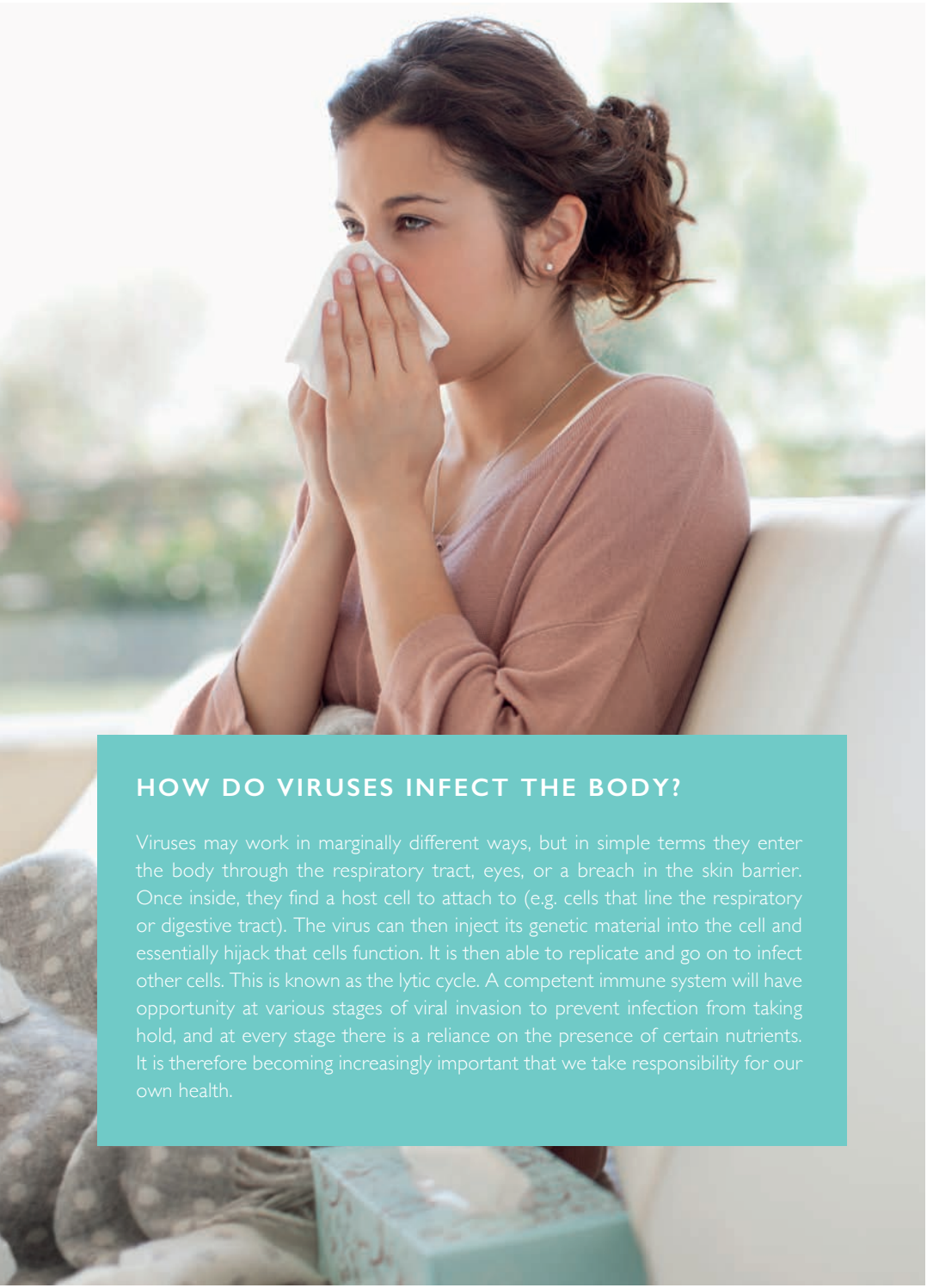
The level of protection afforded by the immune system will vary considerably between individuals, as it can be affected by age, general health, diet, and many aspects of lifestyle. For optimal function, each of the following 6 components should be optimised, and this leaflet will help you to achieve this and also give you tips on how to retain normal health practices in unusual and unexpected situations, such as the recent lockdown.

The 6 main effectors of immune health are: diet, including nutritional status; gut health; sleep; exercise; stress; and toxins (environment or home). Although each area is addressed separately, you will find that each is intertwined with the next. There is also a tips section at the end of the leaflet, which offers further information on how to stay healthy if self-isolating.

Lockdown can be a stressful time in itself - with many having concerns over health, education, finances and the economy, as well as the pressures of staying at home and juggling family life and/or work commitments. Stress can lead us to a vicious cycle of poor health and low immunity. When we are stressed it affects our ability to sleep, which can impact on our exercise and dietary choices. This can further exacerbate stress and poor sleep and cause a downward spiral of health.

This emphasises the need to support all aspects of our health. Supporting our immune function through nutrition is key, but it is also crucial that we pay attention to our physical, mental and emotional wellbeing, as these too play a part in immunity, and in general health.

Read on to understand the role each plays and what you can do to help your immune system "be the best it can".



HOW DO VIRUSES INFECT THE BODY?

Viruses may work in marginally different ways, but in simple terms they enter the body through the respiratory tract, eyes, or a breach in the skin barrier. Once inside, they find a host cell to attach to (e.g. cells that line the respiratory or digestive tract). The virus can then inject its genetic material into the cell and essentially hijack that cells function. It is then able to replicate and go on to infect other cells. This is known as the lytic cycle. A competent immune system will have opportunity at various stages of viral invasion to prevent infection from taking hold, and at every stage there is a reliance on the presence of certain nutrients. It is therefore becoming increasingly important that we take responsibility for our own health.

STEP 1.
IMMUNITY DIET AND NUTRIENTS

As with all systems in our body, our immune system is affected by our dietary choices. Most positive research on health, including immunity and mood, has shown that a Mediterranean-style diet has a myriad of benefits. A Mediterranean diet refers to a diet that is high in vegetables and healthy fats (such as oily fish, olive oil and avocados) and is low in refined carbohydrate and sugar. It also includes moderate protein, fruit and wholegrains. Fresh foods are best for your health, so get the family together and start being creative with cooking. This teaches kids great life skills, provides healthy meals and can be much cheaper than processed or take-away foods. If you are struggling to get hold of ingredients and have some tired vegetables in the fridge, boil them up in a stock and you have a soup which you can freeze.

IMMUNE-SUPPORTING FOODS[1,2]

- Mushrooms
- Dark leafy greens
- Rainbow of coloured vegetables and fruits (limit fruit to 2 per day)
- Garlic, ginger, rosemary and turmeric
- Lemon (add to foods or drink in hot water)
- Fermented foods (e.g. miso, kimchi, kombucha, live yoghurt, sauerkraut)
- Healthy fats such as olive oil, oily fish and avocado

BLOOD SUGAR AND INSULIN[1-3]

Poor regulation of blood sugar and insulin resistance leads to increased levels of insulin, which has been shown to inhibit the immune system. It is also associated with low mood, as well as adrenal dysfunction (linked to stress). It is therefore, essential to ensure blood sugar levels are regulated to support immune and cognitive health.

Blood sugar regulation can be improved by:

- Including healthy fats and protein with each meal, to slow down the release of sugar into the bloodstream
- Ensuring there are adequate levels of nutrients required for blood sugar regulation, such as chromium, magnesium, zinc and alpha lipoic acid
- Time restricted feeding – this is where you fast for at least 12 hours in a 24-hour period and has been shown to reduce insulin levels and improve insulin sensitivity

NUTRIENTS TO SUPPORT MENTAL HEALTH AND WELLBEING

Low mood, depression and anxiety are perhaps heightened during this time, particularly during lockdown or if self-isolating.

You can support your mood with the following:[1,2]

- Tryptophan is a precursor to the feel-good neurotransmitter serotonin. Foods rich in tryptophan include oily fish, turkey, eggs, oats, walnuts and lentils
- Magnesium is involved in the conversion of tryptophan to serotonin and is also considered 'nature's tranquiliser' as it is involved in muscle relaxation. Magnesium-rich foods include dark leafy green vegetables, nuts, seeds and legumes
- Vitamin B6, like magnesium, is an important cofactor for serotonin production. B6 is generally found in oily fish, poultry, wholegrains, most vegetables and legumes
- Vitamin B12 is essential for normal psychological and nervous function. Foods rich in B12 include meat, fish and eggs
- Omega-3 fatty acids - DHA is the predominant omega-3 fatty acid found in the brain and a deficiency is associated with mood disorders. Omega-3 fatty acids can be obtained from oily fish, sea vegetables, flax and chia seeds

VITAMIN D

It may be difficult to obtain adequate levels of exposure to sunshine when you are isolated indoors, so it is important to consider vitamin D levels. Vitamin D deficiency is associated with low mood. Foods such as butter and oily fish are rich in vitamin D, but the best source is sunlight!

THE ROLE OF INDIVIDUAL NUTRIENTS AND SUPPLEMENTS[1,2]

The role that some key nutrients play in supporting the immune system is well-established and there is continuous research emerging on other potential interventions that may provide support against viral infection.

Optimal consumption of the following nutrients discussed would ideally be met through the intake of a well-balanced diet, but this is often challenging to accomplish for many. Insufficient intake of immune-supporting nutrients is, therefore, widespread and often leads to an increased vulnerability to disease and a decrease in resistance to infections. A deficiency in nutrients can impact on various elements of the immune system, such as, causing a decrease in the numbers of lymphocytes; the impairment of phagocytosis and microbial killing; altered production of cytokines; reduced antibody responses and impairments in healing. It is not unexpected then that deficiencies, or even the suboptimal status of nutrients, has seen a correlation with rising levels of morbidity or mortality with regard to viral infection.

As with any intervention, it is important to consider the individual as a whole and therefore use a holistic approach. In the UK, it is estimated that as many as 15 million people live with a chronic or underlying disease and we know that underlying health conditions hold a greater risk of increasing the severity of viral assault. In addition, certain health conditions, such as diabetes and obesity, have been shown to have an adverse effect on micronutrient status.

Pathologies should therefore be considered and supported, as well as simply aiming to optimise immune function. Dysfunctions including inflammation, leaky gut, dysbiosis and insulin resistance should be addressed as these can drive many pathologies and contribute to complications of viral infection.

The following nutrients collectively function to support the immune system.

- **Vitamin C**
- **Vitamin D**
- **Vitamin K**
- **Vitamin A**
- **Zinc**
- **Selenium**
- **Lactoperoxidase**
- **Lysine**
- **Flavonoids**
- **Quercetin**
- **Curcumin**
- **Oregano**
- **N-acetylcysteine**
- **1/3 1/6 Beta Glucans**
- **DHA/EPA**

VITAMIN C

Vitamin C is an essential water-soluble vitamin and is abundant in many foods, particularly citrus fruits and vegetables. The body is not able to store vitamin C, so to maintain adequate levels a daily intake is needed. Vitamin C is a powerful antioxidant and there is extensive research documenting its positive effect on immune function.

Mechanism of Action in Immune Function[1-4]

Vitamin C contributes to our immunity by stimulating and supporting numerous cellular functions of both the innate and adaptive immune system. These include, supporting epithelial barrier function; growth and function of both innate and adaptive immune cells; white blood cell migration to sites of infection; phagocytosis and microbial killing; and antibody production.

Increases Interferon Production – vitamin C aids in the creation of pathogen-fighting interferons. These are proteins that are made and released in response to viruses, bacteria, parasites and cancer cells. Interferons are the first line of defence against viral infection and are likely to be the critical antiviral cytokines in the respiratory epithelial surfaces during the early stages of viral infection.

Stimulates Neutrophils – the exposure of neutrophils to oxidants inhibits their motility. To protect themselves from oxidative damage, neutrophils accumulate millimolar concentrations of vitamins. This results in improved cellular motility and migration in response to chemotactic stimuli and subsequently, enhanced phagocytosis of microbes.

Phagocytes – these are specific cells of the immune system that are able to engulf and kill pathogens.

Supports Lymphocyte Production and Function – lymphocytes can actively accumulate vitamin C against a concentration gradient. Vitamin C has been shown to enhance differentiation and proliferation of B-cells and T-cells, likely due to its gene regulating effects.

Natural Killer Cells – are a type of lymphocyte and can kill virally infected cells. In clinical studies, vitamin C treatment of healthy subjects promoted and enhanced natural killer (NK) cell activity.

Monocytes/Macrophages – it has been shown that monocytes contain a high concentration of vitamin C, which underpins its regulatory role in monocyte and macrophage function. In support of this, an *in vitro* study revealed that intracellular accumulation of vitamin C concentrations could effectively inhibit apoptotic pathways in human monocytes.

Improves Chemotaxis – this is the attraction and movement of macrophages to a chemical signal. Chemotaxis uses cytokines and chemokines to attract macrophages and neutrophils to the site of infection, ensuring that pathogens in the area are killed.

Supports Epithelial Barrier Function – promotes collagen synthesis and protects cell membranes from damage caused by free radicals, thus supporting integrity of epithelial barriers. Vitamin C strengthens the maintenance of the alveolar epithelial barrier and transcriptionally upregulates the protein channels, regulating the alveolar fluid clearance.

COVID-19 and other Viral Infections[5-16]

Vitamin C has beneficial immunomodulating properties in patients with viral infections, predominantly by increasing the production of α/β interferons and down-regulating the production of pro-inflammatory cytokines. Vitamin C deficiency can therefore result in impaired immunity and a higher susceptibility to infection. Patients with acute infectious diseases however, typically have low circulating vitamin C levels (likely due to metabolic consumption). Many reports have shown that viruses can quickly accelerate vitamin C depletion and increase its requirements.

A retrospective cohort study indicated that oral vitamin C reduced the risk of herpes simplex keratitis recurrence, particularly in combination with oral antiviral therapy. High dose IV Vitamin C has also been shown to be effective against other viral infections such as the common cold rhinovirus, avian virus H1N1, and influenza. People deficient in vitamin C are also susceptible to severe respiratory infections such as pneumonia. A recent meta-analysis reported a significant reduction in the risk of pneumonia with vitamin C supplementation, particularly in individuals with low dietary intake. Furthermore, three human controlled trials reported that there was a significantly lower incidence of pneumonia in the vitamin C-supplemented groups.

As of February 2020, a randomised controlled trial (RCT) is being undertaken at the Zhongnan Hospital, that aims to evaluate the clinical efficacy and safety of vitamin C in viral pneumonia from SARS-CoV-2. Researchers hypothesise that vitamin C infusion can improve the prognosis of severe acute respiratory tract infections (SARI). The treatment arm includes a 12g vitamin C infusion for seven days and the primary outcome measures the ventilation-free days. Research has also emerged that treatment with IV vitamin C has potential in reducing inflammation in the lungs and could therefore play a key role in lung injury caused by coronavirus infection.

Furthermore, IV vitamin C has been shown to reduce mortality in patients with sepsis induced ARDS. As of February 2020, the clinical characteristics of patients hospitalized with COVID-19-related pneumonia indicate that 26% were transferred to the ICU because of complications such as ARDS. A further study suggests that more than 40% of individuals hospitalized for severe and critical COVID-19 may develop ARDS. Vitamin C has already been used in hospital ICUs to treat COVID-19 infection and the Shanghai Medical Association have recently

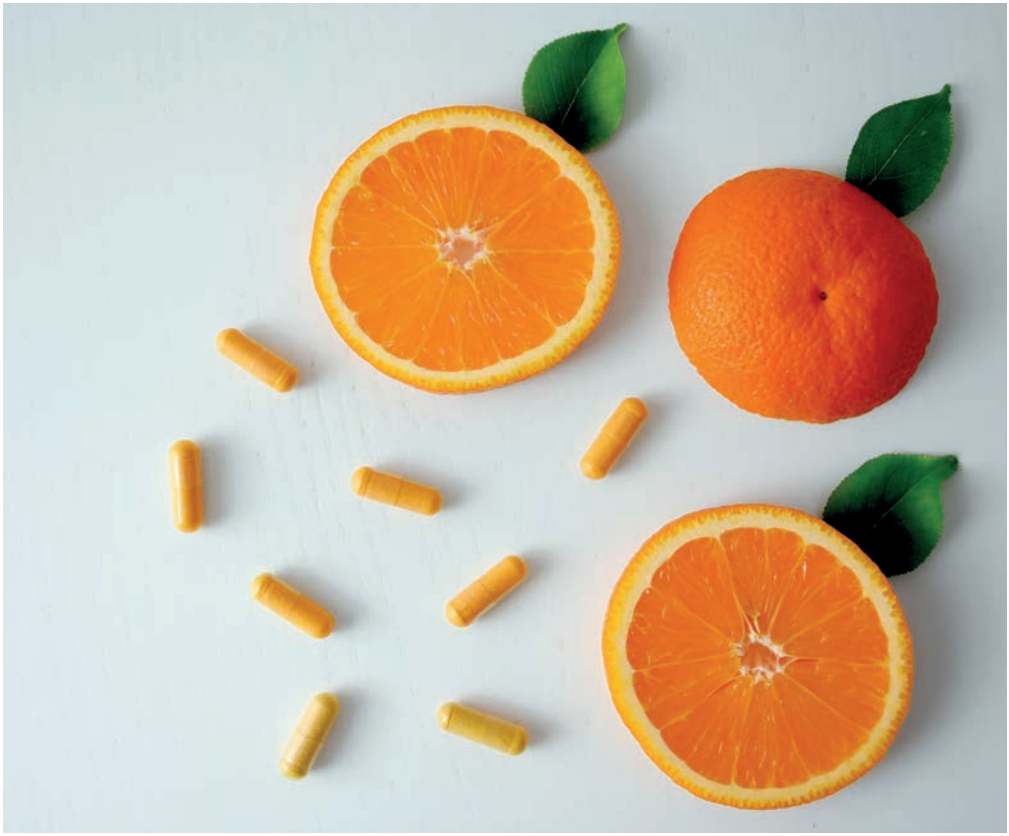
endorsed the use of high-dose vitamin C as a treatment for people with COVID-19. RCT's are currently being undertaken to look at the clinical efficacy and safety of vitamin C for the management of SARI - the severe pneumonia, which is caused by the new coronavirus strain.

With regard to underlying health conditions that may impact on viral progression - research suggests that vitamin C deficiency is associated with a higher risk of mortality from cardiovascular disease (CVD) and may slightly improve endothelial function and lipid profiles in some groups, especially those with low plasma vitamin C levels.

Dosage

Daily intake of at least 500mg/day for healthy individuals. In individuals who are sick, 1–2 g/day in divided doses is recommended.

An average western diet is likely to be giving an intake of 60-300mg Vitamin C per day.



VITAMIN D[1]

Vitamin D is a fat-soluble vitamin and is known to support healthy immune function. Vitamin D has been shown to be deficient in the majority of the population, particularly over the winter months. Obtaining adequate levels during summer-time however, is also subject to many factors (lifestyle, age, sun-cream, ethnicity, weight etc). Recently, there has been a potentially greater risk of deficiency as many of us have been confined indoors during lockdown, particularly if self-isolating. Vitamin D can be manufactured in sunlight by the skin and obtained from the diet. Unlike most essential nutrients however, it is difficult to rely on diet alone to keep levels optimal. Vitamin D is naturally present in very few foods but can be found in oily fish and small amounts in liver, mushrooms, butter, fortified foods and eggs.

A systematic review involving 195 studies in 44 countries reported that 37.3% of studies found that mean values of vitamin D were lower than required. This suggests a potentially widespread negative impact on immune capabilities. The government recommends supplementing 10µg of vitamin D all year round, although requirements may increase depending on vitamin D status. Public Health England have recently increased the recommended level to 25µg/day during the current pandemic.

Mechanism of Action in Immune Function[2-9]

Vitamin D can modulate both the innate and adaptive immune responses. A deficiency in vitamin D is therefore associated with increased autoimmunity as well as an increased susceptibility to infection.

Many immune cells have vitamin D receptors that affect their function, and as such, vitamin D profoundly influences immunity. For example, it promotes differentiation of monocytes to macrophages and increases their killing capacity, modulates the production of inflammatory cytokines, and supports antigen presentation. Vitamin D promotes the expression of potent antimicrobial peptides, which are present in neutrophils, monocytes, NK cells, and the epithelial cells of the respiratory tract.

Specific mechanisms of action in viral infection include, the antiviral immune induction, the modulation of immunoregulatory defence, induction of autophagy and apoptosis, and genetic or epigenetic regulation. Further mechanisms include the stimulation of defensins and cathelicidins. These can decrease the replication of viruses, increase levels of anti-inflammatory cytokines, as well as decreasing concentrations of pro-inflammatory ones that may induce inflammation-related pneumonia, for example. Vitamin D also helps to maintain tight junctions and gap junctions, which help to increase the protective barrier against external threat.

A gene called D3-Upregulated Protein 1 plays a crucial role in directing stem cells to diversify into NK cells, of which one of their functions is to eliminate virus-infected cells. Low vitamin D results in fewer NK cells and impaired innate immune defences against viruses.

COVID-19 and other Viral Infections[3-5,7,8,11,12-27]

Observational studies report an association between low blood concentrations of 25-hydroxyvitamin D and susceptibility to acute respiratory tract infections (ARIs). Further to this, several meta-analyses and systematic reviews have supported the protective role of vitamin D supplementation for the prevention of ARIs.

In particular, a large meta-analysis of 10,933 people from 25 trials in 15 countries investigated whether taking a vitamin D supplement helped to prevent colds, flu and ARIs. It was shown that Vitamin D had a significant protective effect when it was given daily or weekly to people with low vitamin D levels. In another study, level 1 evidence also showed that there was a 12% overall protective effect of vitamin D supplementation against viral ARI, increasing to 19% in those individuals on a daily or weekly regimen of vitamin D. Furthermore, there was a 70% protective effect when vitamin D deficiency was corrected with supplementation. In 2019, an analysis using 21,000 participants from across 8 studies showed that those with a low blood vitamin D level had a 64% increased risk of community acquired pneumonia.

Research suggests SARS-Cov-2 enters cells via ACE2. ACE2 is the host cell receptor responsible for mediating infection by SARS-CoV-2. Coronavirus viral replication downregulates ACE2, dysregulating the renin-angiotensin system (RAS) and can lead to a 'cytokine storm' in the host, potentially causing ARDS. ARDS involves acute inflammation of the lungs and causes widespread damage to the alveoli (tiny sacs that help to process gases during respiration). Vitamin D enhances cellular immunity, potentially in part by reducing the cytokine storm induced by the innate immune system. It does so by helping to signal the increased production of anti-inflammatory molecules and decrease the production of pro-inflammatory ones.

Vitamin D is also known to mitigate the scope of acquired immunity and regenerate endothelial lining. This may also be beneficial in minimising the alveolar damage caused in ARDS. Further research shows that Vitamin D acts to rebalance RAS and attenuates lung injury. Additionally, chronic vitamin D deficiency induces lung fibrosis through activation of the RAS.

Geographical Considerations[19,27]

After studying global data, researchers discovered a strong correlation between severe vitamin D deficiency and mortality rates. Northwestern University researchers conducted a statistical analysis of data from hospitals and clinics across China, France, Germany, Italy, Iran, South Korea, Spain, Switzerland, UK and the USA. They found that patients from countries with high COVID-19 mortality rates, such as Italy, Spain and the UK, had lower levels of vitamin D compared to patients in countries that were not as severely affected.

Moreover, a literature search was conducted on the vitamin D status in older adults in European countries affected by COVID-19 infection. The infection and mortality data were gathered primarily from the World Health Organisation. Results demonstrated that lower latitude and typically 'sunny' countries such as Spain and Italy had low mean concentrations of 25(OH)D and high rates of vitamin D deficiency. These countries have also been experiencing the highest infection and death rates in Europe. The northern latitude countries (Norway, Finland, Sweden) which receive less UVB sunlight than Southern Europe, actually had much higher mean 25(OH)D concentrations, low levels of deficiency and for Norway and Finland, lower infection and death rates. Interestingly, countries with a formal vitamin D fortification policy appeared to have the lowest rates of infection, whilst countries with no policy and highest deficiency rates appeared to be more adversely affected.

Globally, COVID-19 was seen to dominate in the northern hemisphere, which had just come out of winter, when vitamin D levels are known to be reduced. An anomaly to this is Japan. Japan is an outlier in the north, with only a very mild outbreak and has the lowest incidence of Vitamin D deficiency, perhaps in part to its high fish consumption.

An Indonesian Study[21]

A retrospective cohort study was carried out, which included two cohorts (active and expired) of 780 cases with laboratory-confirmed infection of SARS-CoV-2 in Indonesia. Age, sex, co-morbidity, vitamin D status and mortality were extracted from electronic medical records. The aim was to determine patterns of mortality and associated factors, with a special focus on Vitamin D status. Results revealed that the majority of the death cases were male and older, had pre-existing conditions and below normal vitamin D serum levels. Key findings were that when controlling for age, sex and comorbidity, vitamin D status is strongly associated with COVID-19 mortality.

The Irish Longitudinal Study on Ageing[20]

The prospective study – TILDA, has been observing and measuring parameters in adults aged 50 years and older and has a wealth of data with regard to the vitamin D status of its participants. Researchers have subsequently released a crucial report in response to the COVID-19 pandemic. The report found that Vitamin D played a critical role in preventing respiratory infections and boosting the immune system response to infections. Findings from the report were that during the winter period, 21.3% (244,209) of adults aged >55 years were found to be vitamin D deficient. The highest rates of deficiency were observed for those aged 80-84 years (29.6%; 23,987) and those aged >85 years (46.6%; 31,480). Significantly higher rates of vitamin D deficiency were seen in those that were obese or with chronic lung disease, both of which have been observed to make individuals vulnerable to COVID-19. Overall, the study demonstrates that of those aged 55+, 1 in 5 are vitamin D deficient during the winter and 1 in 12 during the summer.

Comorbidities

Vitamin D deficiency is associated with many comorbidities related to COVID-19 case fatalities. Obesity and related conditions seem to worsen the effects of COVID-19. A body mass index ≥30 is associated with lower serum vitamin D levels compared with non-obese individuals meaning that people who are obese may need larger than usual intakes of vitamin D to achieve levels comparable to those of normal weight. A growing body of evidence also suggests that vitamin D might play some role in the prevention and treatment of type 1 and 2 diabetes, hypertension and glucose intolerance, which are known to increase the severity of viral infection.

Dosage

Approx. 30-40µg per day

For those who have never supplemented or who have family history of osteoporosis and/or respiratory infections the dose can be up 100µg per day for short-term use. We recommend blood levels are checked and anyone taking a high dose for over 8 weeks includes vitamin K2 and magnesium alongside.

An average Western diet is likely providing a daily intake of around 3µg of vitamin D.

VITAMIN K

Vitamin K refers to a group of fat-soluble vitamins, which can be split in to two groups - vitamin K1 (phylloquinone) and vitamin K2 (menaquinone). K1 is found predominantly in plant foods such as dark, leafy vegetables and K2 can be found in animal foods. Average diets are usually not lacking in vitamin K.

Mechanism of Action in Immune Function1

Vitamin K is important for bone metabolism, regulating blood calcium levels and is probably best known for its blood clotting properties. It can also act as a cofactor for some plasma proteins, thereby affecting immune and inflammatory responses particularly mediated by T-cells. Studies have found links between vitamin K levels and disease, including, inflammatory diseases, CVD and cancer.

COVID-19 and other Viral Infections[2,3]

Patients with severe COVID-19 are more likely to have comorbidities such as Type 2 diabetes, hypertension and CVD, which are also associated with reduced vitamin K status. Recently, it was hypothesized that improving vitamin K2 status is linked to better health outcomes with regards to cardiovascular and lung health, and therefore improved COVID-19 outcomes. Researchers proposed an association between low levels of vitamin K and the enhanced breakdown of tissue fibres, such as elastin, which is involved with pulmonary disease. Vitamin K status was evaluated in 123 patients with COVID-19 and 184 controls. Measurements showed that dp-ucMGP (inactive Matrix Gla-protein - which is a vascular calcification inhibitor that needs vitamin K for its activation) was significantly lower in COVID-19 patients compared to controls. Dp-ucMGP levels were also significantly lower in COVID-19 patients with unfavourable outcomes compared to those with less severe disease – all pointing towards a link between vitamin K deficiency and disease severity. Also, low dp-ucMGP levels were significantly correlated with desmosine levels, a measure of the breakdown of elastin. The findings suggest that improved vitamin K levels may play a role in improving the body's natural ability to cope with the novel virus. With regard to underlying health conditions - in another study, adequate vs. inadequate vitamin K intakes were associated with a 22% lower risk of CVD-related mortality and a 15% lower risk of all-cause mortality. The report also indicated that, while over two-thirds of individuals with chronic kidney disease had vitamin K intakes below the adequate intake, the risk of CVD mortality was 41% lower in those with adequate compared to suboptimal intakes.

Dosage

60-100µg K2/day

VITAMIN A

Vitamin A is a fat-soluble vitamin and is important for many processes in the body, including maintaining healthy vision, aiding growth and development and supporting the normal functioning of the immune system. There are two different types of vitamin A - preformed vitamin A (found in meat, poultry, fish, and dairy), and provitamin A (found in red, yellow and orange-coloured fruits, dark leafy vegetables etc). The most common type of provitamin A in food is beta-carotene.

Mechanism of Action in Immune Function[1-4,7]

The immune-supporting roles of vitamin A include, the promotion of mucins and keratins, lymphopoiesis, apoptosis, cytokine expression, antibody production; and the enhanced functions of neutrophils, NK cells, monocytes or macrophages.

Vitamin A plays an important role in the maintenance and repair of the body's natural defences, which includes the mucosal barriers in the respiratory and digestive tract. These help to trap bacteria, viruses and other infectious agents. Deficiency can impair innate immunity by impeding the normal regeneration of epithelial tissue damaged by infection.

Vitamin A is also required for adaptive immunity and plays a role in the development of both T-helper cells and B-cells (type of white blood cells that helps identify pathogens). Vitamin A is known as an anti-inflammation vitamin because of its critical role in enhancing immune function.

COVID-19 and other Viral Infections[1,5-10]

Those deficient in vitamin A are prone to the increased risk, severity, and impaired immune response to viral infection, including the respiratory syncytial virus, measles virus, and the influenza virus.

Measles can become severe in vitamin A-deficient children. The mechanism by which vitamin A inhibits measles replication is by upregulating elements of the innate immune response in uninfected bystander cells, making them refractory to infection during subsequent rounds of viral replication. Vitamin A supplementation has also been shown to reduce the life-threatening complication of pneumonia after acute measles infection. Even children who are only mildly deficient in vitamin A have a higher incidence of respiratory complications and diarrhoea, as

well as a higher rate of mortality from measles infection compared to children consuming sufficient vitamin A.

Vitamin A deficiency causes pathological alterations in the epithelium of the respiratory tract, including keratinization and loss of ciliated cells, mucus, and goblet cells. Clinical vitamin A deficiency can therefore be associated with lower respiratory-tract infections.

In animal studies, the effect of infection with infectious bronchitis virus (a type of coronavirus) was more pronounced in chickens fed a diet marginally deficient in vitamin A than in those fed a diet adequate in vitamin A.

Low plasma or serum vitamin A levels have been described in all stages of HIV infection and among many different risk groups.

In relation to conditions that may exacerbate viral infection, research further shows carotenoids' antioxidant and anti-inflammatory activity may help balance CVD factors, healthy blood pressure and insulin sensitivity.

Dosage

5,000IU/day – up to 15,000IU acutely for short-term use (but not to be used in those who smoke or who have ever smoked heavily)

As vitamin A is a fat-soluble vitamin, it can be stored in the body, which means that excess consumption can lead to toxic levels.

Average non-vegan diets are likely to give 100IU of Vitamin A per day.

ZINC[1,2]

Zinc is an essential mineral that is naturally present in many foods such as red meat, poultry, fish, wholegrains, dairy, nuts and legumes. The body does not store excess zinc, so it must be consumed regularly in the diet. A deficiency in zinc is common is a modern-day diet. Zinc is involved in numerous processes, including growth and development, wound healing, gene expression, protein synthesis and more. It is particularly involved in multiple aspects of immune function and provides vital contributions to most enzymatic functions in the human body. There is now an abundance of evidence that has accumulated, which demonstrates the activity of zinc against a variety of viruses, and via numerous mechanisms.

Mechanism of Action in Immune Function[1, 3, 19]

Zinc is crucial for the normal development and function of cells mediating nonspecific immunity such as neutrophils and NK cells and also plays a role in the development of acquired immunity.

Zinc supports the communication between immune cells and because of its important role in immune function, it is often added to nasal sprays and lozenges. Perhaps most importantly in relation to coronavirus, zinc is a modulator of the production of inflammatory cytokines.

Zinc deficiency can result in impaired formation and activation of lymphocytes, disturbance of the intercellular communication via cytokines and a weakening of the innate host defence. In short, zinc deficiency increases susceptibility to infectious diseases and is associated with reduced:

- T-cell and B-cell function
- Intracellular killing
- Apoptosis (programmed cell death)
- Cytokine production
- Lymphoproliferative response to mitogens
- Thymic hormone levels
- Phagocytosis
- Chemotaxis
- Cytotoxic activity

COVID-19 and other Viral Infections[1-19]

There is a large body of evidence that shows zinc has strong antiviral activity against various viruses and that it can suppress viral attachment and replication. Studies have demonstrated that zinc deficiency impairs antiviral immunity, particularly to the herpes simplex virus, the common cold, hepatitis C and the human immunodeficiency virus (HIV). Supplementation with zinc is supported by evidence that not only does it help prevent viral infection but reduces the severity and duration. A meta-analysis of oral zinc supplementation studies show that zinc has beneficial effects on the shortening of symptom duration of the common cold infection.

It has also been demonstrated that intracellular levels of zinc can efficiently impair the replication of a variety of RNA viruses, including poliovirus and influenza virus. Other *in vitro* studies have also supported findings that zinc can help reduce the viral replication of viruses including severe acute respiratory syndrome (SARS).

Metallothionein's (MTs) are small, cysteine-rich proteins characterized by a high affinity for monovalent and divalent cations, such as copper and zinc. MT expression is well documented in the context of viral infection. Antiviral effects of zinc treatment against hepatitis C *in vitro* was mediated through MT induction, suggesting that zinc may facilitate the antiviral role of MTs against other viruses.

Viruses, such as HIV, use the enzyme reverse transcriptase to hijack the cell's DNA to replicate. Without it, the viral genome would not incorporate into the host cell, resulting in failure to replicate. Although coronavirus does not appear to use the same mechanism to enter cells, reverse transcriptase inhibitors have been highlighted as potential candidates for the treatment of COVID-19, with some improvements of symptoms reported. Zinc has been shown to inhibit reverse transcriptase.

Positive-stranded RNA viruses include many pathogens, including SARS CoV coronaviruses. They have evolved a variety of replication strategies, but are unified in the fact that an RNA-dependent RNA polymerase functions as the core enzyme of their RNA-synthesizing machinery. Coronaviruses utilise the enzyme SARS-CoV RdRp where elongation of which was inhibited and template binding reduced by the presence of zinc *in vitro*. Zinc ionophore also demonstrated to block the replication of SARS CoV in cell culture *in vitro*.

Further research suggests SARS-Cov-2 virus enters cells via ACE2 by binding to zinc metalloproteases. Coronavirus viral replication downregulates ACE2. Zinc is an essential component of ACE2 receptors, and therefore may help to normalise ACE2 receptor function.

Zinc has been shown to reduce the risk of lower respiratory infection, which may be of particular significance in the context of COVID-19. Furthermore, a meta-analysis of RCTs demonstrated that zinc supplementation in children is associated with a reduction in the incidence and prevalence of pneumonia. Zinc deficiency is however common, particularly in those populations most at risk for severe COVID-19 infections.

Comorbidities

A systematic review showed that zinc supplementation improved insulin resistance in obese individuals. Furthermore, a meta-analysis demonstrated that serum zinc levels were significantly lower in obese children and adults. Findings from another recent meta-analysis also supported the notion that zinc supplementation may have clinical potential as an adjunct therapy for preventing or managing diabetes. In addition, a study explored the relationship between serum zinc levels and heart failure by using a meta-analysis approach. A significant association between low serum zinc levels and heart failure was found.

Dosage

Daily intake of 5-15mg is recommended

Up to 30mg/day acutely for short-term use

Most people are ingesting around 7-11mg/day Zinc

SELENIUM[1,2]

Selenium is an essential trace mineral and adequate levels are important for the effective functioning of our immune system. The concentration of selenium in plants (and thus the food chain) is determined by the content and availability of the selenium in the soil. In the UK, the selenium content of the soil is generally low and in the majority of age groups in the UK, the reported mean selenium intake is below the RNI. Selenium intake in the UK has fallen over the last 25 years and recent surveys indicate that average selenium intake may be as low as 30–40 µg/d. Interestingly, statistics are showing that mortality rates from influenza have steadily risen over the last two decades. Selenium can be found in Brazil nuts, cashew nuts, sunflower seeds, grains, oily fish, eggs and seaweed.

Mechanism of Action in Immune Function[3-5]

Selenium is an essential antioxidant and also supports the production of the master intracellular antioxidant - glutathione. As the integral part of several selenoproteins, including the glutathione peroxidases and thioredoxin reductases, selenium has a critical role in the defence against viral infection through its antioxidant, redox signalling, and redox homeostatic contributions.

Selenium-deficient lymphocytes are less able to proliferate in response to mitogen, and in macrophages, leukotriene B4 synthesis (which is essential for neutrophil chemotaxis) is impaired. One of the most widely investigated associations between selenium and the immune system is the effect on neutrophil function. Neutrophils from selenium-deficient mice, rats and cattle are able to ingest pathogens *in vitro* but are less able to kill them than are neutrophils from the selenium-sufficient animal.

Studies have further demonstrated an enhancement of both cell-mediated and humoral immune responses by increasing levels of selenium intake. Selenium deficiency can cause oxidative stress in the host and can alter a viral genome so that a normally benign or mildly pathogenic virus can become highly virulent.

Viral Infection[no]

Our immunity to viruses is compromised if selenium intake is low and viruses can exploit this by replicating and mutating. It is of no surprise therefore, that selenium deficiency has been associated with the pathogenicity of several viruses. In one study, benign strains of Coxsackie

and influenza viruses were shown to mutate to highly pathogenic strains in a selenium deficient host. A further study demonstrated that replication of a mild strain of influenza virus in selenium deficient mice resulted in a novel virulent strain that caused severe lung pathology. These studies demonstrate that the selenium status of the host can profoundly influence the genome of the viral pathogen, leading to a new viral strain. Further data from animal models and epidemiological studies in humans indicate that a deficiency in selenium can lead to reproducible genetic mutations and increased virulence of certain viruses. The nutritional status of the host should therefore be considered when studying the mechanisms underlying the evolution of emerging viruses.

Human studies have investigated the relationship between selenium and viral infection in terms of immune function and viral handling. One study reported an increase in immune function following challenge with influenza virus in 725 elderly subjects supplemented with 100µg/day of selenium. In an RCT in the UK, supplementation with selenium (50 and 100µg/day) augmented the cellular immune response to live attenuated poliovirus through increased production of interferon-γ and other cytokines, and earlier peak T-cell proliferation, compared to placebo. The 100µg/day group showed a significantly greater T-cell response. Furthermore, a more rapid clearance of poliovirus was seen in the selenium supplemented groups and there were fewer mutations in the viral genome than occurred in the placebo group.

The Impact of Selenium Status on the Virulence of COVID-19[13]

Although to date (May 2020), selenium has not been tested on COVID-19 itself, it is likely to exert similar mechanisms of action as it does with other viruses. Research over 25 years has shown that in hosts that have low selenium intakes/blood plasma levels, viruses are likely to be much more severe in their attack, often leading to lung problems and even death.

Stemming from previous research and the belief that the low intake of selenium is a factor in the increased incidence of chronic conditions and susceptibility to viral infections, research has been collated which compares global selenium intake levels between populations. The aim was to evaluate if there was a correlation between selenium intake among populations and the incidence of, and mortality from COVID-19.

The data collated for high and low selenium countries covered 11% of the world's population and accounted for 63% of the deaths.

The following statements can be inferred from the results:

Virulence of COVID-19

Deaths per million in the low selenium areas is 227 and is 28 times higher than high selenium areas at 8 deaths per million.

Protection from catching COVID-19

Results show that you are much less protected from COVID-19 in low selenium intake areas. At 2,236 cases per million you are 11 times more likely to catch COVID-19 than the high selenium intake areas, at 194 cases per million.

Severity once you catch it

Deaths divided by number of positive tests.

Results show that if you do catch COVID-19 in a low selenium intake area you are 2.5 times more likely to die than somebody who catches it in a high selenium intake area.

In summary, selenium intake/selenium blood plasma levels and selenium soil content are very good predictors for immunity and protection against COVID-19.

Selenium Status and Reported Outcome of COVID-19 Cases in China[14]

Margaret Rayman, a professor of Nutritional Medicine at the University of Surrey, and a team of researchers hypothesised that selenium status was associated with COVID-19 disease outcome in China. Rayman has previously highlighted the importance of selenium for many conditions including CVD and cancer, as well as highlighting the incidence of selenium deficiency across Europe. This latest pandemic has motivated her to revisit her previous work on selenium function and deficiency. She has proposed that the appearance of COVID-19 in China could be linked to the belt of selenium deficiency that runs from the north-east to the south-west of the country. Her team of researchers subsequently carried out a population-based, retrospective analysis, which examined data from provinces and municipalities with more than 200 cases, and cities with more than 40 cases. In the city of Enshi in Hubei Province, which has the highest selenium intake in China, the cure rate was almost three-times higher than the average for all the other cities in Hubei Province. By contrast, in Heilongjiang Province,

where selenium intake is among the lowest in the world, the death rate from COVID-19 was almost five-times as high as the average of all the other provinces outside of Hubei. Despite being unable to control for all confounding factors and various limitations to the study - they found that areas with high levels of selenium were more likely to recover from the virus and therefore there was an association between the reported cure rates for COVID-19 and selenium status.

Dosage

Selenium is a nutrient of which being in the correct form is vital for bio-efficacy and also safety. The less used form but most bio-effective is selenium from yeast, which has GRAS status, and was evaluated by EFSA. This form of selenium has the appropriate amino acids attached for incorporation quickly into the human seleno-proteins.

150-200µg per day selenium yeast

Average Western diets are providing around 55µg/day selenium

LACTOPEROXIDASE

The inhalation of pathogens is the primary route for infections that affect the respiratory system. Viruses are spread via tiny droplets or particles and have the potential to live on surfaces long enough to penetrate the mucosal epithelium. The epithelium of the respiratory tract provides a physical barrier to viruses and is therefore one of the first lines of defence utilised by the body to ward off infectious agents. This makes innate airway defences crucial in preventing illness from taking hold. An effective defence is reliant on many factors such as communication with the adaptive immune system and the secretion of epithelial defence molecules.

Lactoperoxidase (LPO) is an enzyme that is found in our exocrine secretions and is well known for its antimicrobial activity. Glands that secrete LPO include the mammary, salivary and mucosal glands, thus making LPO present in milk, saliva, tears and the epithelial surfaces of the respiratory and gastrointestinal tract.

Mechanism of Action in Immune Function[1-5]

LPO is a natural antimicrobial agent and one of the body's first lines of defence against pathogens. The LPO system is a combination of LPO, thiocyanate (or iodine) and hydrogen peroxide and makes up part of the humoral immune response. The mechanism of action is the oxidation of thiocyanate ions with the use of hydrogen peroxide to form hypothiocyanite ions. Hypothiocyanite exerts a wide spectrum of activity against bacteria (gram positive and gram negative), viruses, yeasts and moulds. It does so by oxidizing the thiol groups of amino acid residues of microbial proteins, leading to impaired function, inhibition of cell division or death of the microorganism.

LPO is present in human milk throughout lactation and contributes to its protection against pathogens. With regard to oral health, the LPO system regulates the composition of microflora and prevents the growth of pathogenic microorganisms present in periodontitis. LPO also plays an important role in protecting the respiratory and digestive tract.

How well the innate system functions however, is heavily dependent on our nutritional status and can be compromised if our diet is poor. Nutrients can be tailored specifically to influence the response of the host and the following can help to facilitate LPO.

Iron

LPO is an iron containing glycoprotein and therefore dependent on adequate levels of iron in the body. Iron deficiency is the most common nutritional disorder in the world, therefore having widespread potential implications for innate system competence. Ensuring adequate levels of iron are met can help to optimise LPO. Rich sources of iron include red meat, legumes, pumpkin seeds, spinach and kale. Vitamin C has been shown to enhance iron absorption so including vitamin C rich foods such as citrus fruits and dark leafy vegetables will help to promote absorption.

LPO uses either thiocyanate or iodine as its substrate, of which it oxidises.

Thiocyanate

Thiocyanate is found in plant foods such as kale, cabbage, cauliflower, Brussel sprouts and turnips. It can also be derived from plants containing cyanogenic glycosides such as almonds, linseed and beans. A shift in our dietary patterns over the last few decades towards processed foods and away from natural foods has seen a potential widespread reduction in the consumption of thiocyanate-containing foods.

Iodine

Iodine deficiency is common and is often related to poor soil quality. Crops grown in low iodine soil will impact on the plants, animals that eat the plants and subsequently humans. On a global scale, iodine deficiency is a serious public health problem, and it is estimated that 2 billion people worldwide have insufficient dietary iodine intakes. Many countries have adopted a mandatory salt iodisation programme to ensure iodine is in the public food chain, although this has never been adopted by the UK. Iodine is present in fish/shellfish, eggs, nuts, meat, dairy and seaweed. Again, a shift away from natural foods has further caused a decline in the levels of iodine ingested. Those that follow a Vegan, Vegetarian or dairy-free diet may be at particular risk of insufficient iodine intake.

EFSA recommendations of 150µg/day for adults

On average we get 180µg /day from diet and need 280µg /day for optimal health

COVID-19 and other Viral Infections[6-13]

Hypothiocyanite has powerful anti-viral capabilities as it has been shown to oxidize the sulfhydryl groups often present on the outer structure of viruses rendering them damaged or destroyed. By oxidizing free thiol radicals of proteins and creating disulphide bonds hypothiocyanite seems capable to alter the surface proteins of respiratory viruses, preventing their binding with the airway epithelium. It is also argued that hypothiocyanite might disturb the synthesis and assemblance of viral proteins and nucleic acids, thereby interfering with the release of viruses from infected cells.

One study showed that the H1N2 influenza virus was inactivated by human and rat tracheal epithelial cells. The LPO system which produced hypothiocyanite showed a potent anti-influenza mechanism which inactivated the virus prior to infection of the epithelium. More recently, another study showed that LPO was capable of inactivating 12 different influenza strains when tested *in vitro*. A recent laboratory experiment also demonstrated that the hypothiocyanite ion inactivated viral activity *in vitro* against the 2009 H1N1 pandemic influenza virus. Further research also supports LPO and its antiviral capabilities. The lack of an LPO system in nasal and eye secretions of humans may explain the survival and shedding of some bacteria and viruses from mucosal secretions.

The LPO system can be mimicked and enhanced using exogenous LPO, an approach originally developed to sterilise milk, but which is now being used by increasing numbers of healthcare professionals to treat clinical infections.

Research findings have shown hypothiocyanite to be an important and active molecule against a range of viruses and an important participant in the antiviral defences of the innate immune system. This may suggest its wider potential application for newly emergent strains such as the SARS-CoV-2.

LYSINE

Lysine is an essential amino acid and is found in foods that are rich in protein such as meat, cheese, fish and eggs. It must be included in the diet as the body is unable to synthesise it. Lysine is important for carrying out many roles in the body including ones related to the immune system.

Mechanism of Action in Immune Function[1-5]

Amino acids, including lysine, are building blocks for proteins, which are needed for the production of immune cells. Amino acids play an important role in the pathogenesis of all virus-related infections, both as basic substrates for protein synthesis and as regulators in many metabolic pathways, including gene expression.

Studies have demonstrated an important role for amino acids in immune responses by regulating: 1 – the activation of T lymphocytes, B lymphocytes, NK cells and macrophages; 2 – cellular redox state, gene expression and lymphocyte proliferation; and 3 – the production of antibodies and cytokines.

Research has demonstrated that lysine is capable of strengthening the immune system and exhibits anti-viral properties. For example, it has been shown to have positive effects on the herpetic family of viruses which include Herpes (HSV-1), Epstein Barr and Kaposi's sarcoma. Virus replication strongly depends on host metabolic machinery and essential cellular factors, in particular, on amino acid profiles.

Lysine has shown significant improvement in both the rate and quality of wound healing. In one study, treated wounds showed a remarkable thickening of the dermo-epidermal layer, suggesting increased cell proliferation from the basal layer.

Lysine regulates inflammatory immune responses (inhibits TNF and IFN) has been shown to increase the absorption of zinc, and therefore helps to further support the body's immunity.

COVID-19 and other Viral Infections[6-15]

Lysine & Arginine

It is essential to look at the relationship that exists between lysine and arginine to gain a better understating of the function of lysine on viral infection.

Lysine and arginine share the same biological pathway and both compete for entry in to the cell. Many studies have demonstrated that some viruses rely on arginine for their survival and that arginine is an essential requirement for their replication and progression. Lysine is thought to be effective against some viruses as it blocks arginine and hence viral replication.

There are several mechanisms by which lysine functions: it competes with arginine for reabsorption at the renal tubule, thereby increasing arginine excretion; it competes for intestinal absorption; it induces the enzyme arginase, resulting in degradation of arginine; and it competes for transport into cells.

When arginine is not available, herpes viruses are unable to complete a single replication cycle and cell damage is evident in infected cells. Other studies show that Lysine has a positive effect on HSV-1 infection, symptoms and occurrence and further studies support lysine supplementation on the reduced recurrence rate of HSV-1 infections.

In addition, excess nitric oxide from arginine can become peroxynitrate, which has been shown in some cases to increase infection. Although there has been contrasting results in other research, one study concluded that nitric oxide together with O2 may be the most important pathogenic factors in influenza virus-induced pneumonia in mice. Another study showed that the severity of the flu virus increased with a greater amount of nitric oxide. Lysine is therefore indicated in limiting nitric oxide by regulating arginine. A decrease in respiratory infections has positively been associated with Lysine.

It is worth noting that a high intake of Lysine has potentially been associated with increasing the risk of high viral load, subsequent acceleration of immunosuppression and HIV progression.

Dosage

Typical therapeutic dosage of lysine for herpes infections is 1-1.5 grams/day

FLAVONOIDS[1,2]

Flavonoids are a diverse group of phytonutrients and have several subgroups, which include anthocyanidins, chalcones, flavones (including luteolin and apigenin), flavanols (catechins), flavonols (e.g. quercetin and kaempferol), and isoflavones (genistein and daidzein). The main function of flavonoids is to protect plants and they are often responsible for the bright colours in fruits and vegetables. They are also present in some plant products such as tea, red wine and chocolate. In humans, they provide many benefits including antioxidant, anti-inflammatory and antiviral capabilities.

Mechanism of Action in Immune Function[3]

More than 4000 flavonoids have been identified, and their activity in humans is diverse - from regulating cellular activity and fighting off free radicals, to modulating enzyme activities, modifying gene expression and inducing cellular apoptosis.

COVID-19 and other Viral Infections[1, 4-10]

Research has shown that flavonoids from Pterogyne Nitens could inhibit the entry of the hepatitis C Virus.

The anti-coronavirus activity of some flavonoids (herbacetin, rhoifolin and pectolinarin) was due to the inhibition of 3C-like protease.

Other flavonoids (isobavachalcone, quercetin 3-β-d-glucoside, and helichrysetin) were also able to block the enzymatic activity of MERS-CoV/3CLpro. Bioflavonoids from Torreya nucifera also had an inhibitory effect on SARS-CoV/3CL. SARS-CoV 3C-like protease plays an important role in viral replication.

Data shows the possibility that TGG and luteolin may achieve their antiviral activity by interfering with the virus-cell fusion process against SARS-CoV. Quercetin is an analogue of luteolin, which is structurally related, and is FDA approved. It has additionally demonstrated anti-viral properties potentially via the same mechanism.

Several flavonoids were tested for their potential to regenerate and promote the hypothiocyanite production by lactoperoxidase with positive results. Because of their antioxidant and anti-inflammatory behaviour, flavonoids are associated with CVD prevention. Results of a meta-analysis carried in 2018 also suggests that a high intake of dietary flavonoids correlates with a lower risk of type 2 diabetes.

QUERCETIN[1]

Quercetin flavanols are the most abundant of the flavonoid molecules and are widely distributed in plants. They are therefore found in an array of foods including apples, blueberries, broccoli, grapes, onions, tomatoes and green tea, as well as many nuts and seeds.

Mechanism of Action in Immune Function[1-4]

In vitro and some animal models have shown that quercetin has a wide range of biological actions including anti-carcinogenic, anti-inflammatory and antiviral activity.

Quercetin has been shown to have antiviral effects against both RNA (e.g. influenza and coronavirus) and DNA viruses (e.g. herpesvirus). It also has a role as an antioxidant and anti-inflammatory, modulating signalling pathways that are associated with post-transcriptional modulators affecting post-viral healing.

Several studies *in vitro*, using different cell lines have shown that quercetin inhibits lipopolysaccharide (LPS) induced TNF-α production in macrophages, and LPS-induced IL-8 production in lung cells.

Quercetin can inhibit viral replication at various stages: Inhibition of PI-3 kinase (an enzyme required for viral endocytosis); transcription of viral genome by inhibiting RNA polymerase 3D POL (which is required for negative-strand RNA production); and inhibits viral protein translation by promoting cleavage of eIF4G. At the same time quercetin also increases viral clearance by enhancing mitochondrial antiviral responses.

Viral Infections[1, 5-15]

Quercetin promotes viral eradication or inactivation, and the inhibition of viral replication, particularly in the early stages, such as during viral attachment and viral-cell fusion.

The literature on quercetin is supportive of the anti-pathogenic capacities of quercetin when it is cultured with target cells and a broad spectrum of pathogens including upper respiratory tract infection (URTI) related rhinoviruses, adenoviruses and coronaviruses.

A study demonstrated that quercetin showed inhibitory activity in the early stage of influenza infection and was effective against a wide spectrum of strains. Furthermore, quercetin has also been shown to reduce viral internalization and replication *in vitro*; and viral load, lung inflammation and airways hyper-responsiveness *in vivo*. A systematic review was carried out

to assess the efficacy of dietary flavonoids on URTIs and immune function in healthy adults. Overall, flavonoid supplementation decreased URTI incidence by 33% compared with control, with no apparent adverse effects.

A further study found that the flavonoid derivative quercetin 3-β-O-d-glucoside had the ability to protect mice from Ebola even when given as little as 30 minutes prior to infection. Furthermore, the study demonstrated that the compound targets the early steps of viral entry. In addition, a study demonstrated that Q3G (a natural derivative of quercetin) exerts antiviral activity against ZIKV in both tissue culture and knockout mice, and that post-exposure in vivo treatment with Q3G could have a beneficial effect.

Quercetin has been shown to favourably modulate viral-induced pathological cellular processes via the modulation of NLRP3 inflammasome activation. Moreover, it promotes resolution of collateral damage and restoration of function by modulation of mast cell stabilization (anti-fibrotic). Additionally, quercetin reduces rhinovirus-induced expression of pro-inflammatory cytokines and lung inflammation in mice and was also found to reduce viral load and improve lung function in a mouse model of chronic obstructive pulmonary disease.

Quercetin has shown strong potential to act as a coronavirus inhibitor, providing support for regulating the body's inflammation response to virus. Some studies have also found quercetin to improve survival and decrease cell damage in a mouse model of sepsis.

In relation to underlying health conditions that may increase the severity of viral infection, diet supplementation with combinations of flavonoids was shown to reduce CVD risk factors in humans. Another study found that a diet rich in flavonoids - including quercetin, anthocyanins and catechins - was associated with significantly lower mortality from coronary heart disease.

Dosage

250-500mg

Diets high in onions and apples - the best sources of quercetin, will be providing around 300mg/day.

CURCUMIN [1]

Curcumin is a lipid-soluble polyphenol and the main active ingredient of *Curcuma longa* (turmeric). It has powerful anti-inflammatory effects and is a strong antioxidant. Curcumin is not well absorbed so it is beneficial to consume with black pepper, which contains piperine, and can enhance the absorption by up to 2,000%.

Mechanism of Action in Immune Function[2-8]

Curcumin enhances the immune system, helps decrease viral growth and can reduce symptoms. Accumulated research has suggested that curcumin can play an inhibitory role against numerous viruses. These mechanisms involve either a direct interference of viral replication machinery or suppression of cellular signalling pathways, which are essential for viral replication.

Curcumin has been shown to modulate the NLRP3 inflammasome. The NLRP3 inflammasome is a protein complex that initiates an inflammatory form of cell death and triggers the release of proinflammatory cytokines. The NLRP3 inflammasome has been implicated in a wide range of diseases, including infectious disease.

COVID-19 and other Viral Infections[9]

Curcumin has been shown to reduce inflammation and decrease viral activity for COVID-19. A preprint suggests that curcumin can target the COVID-19 main protease to reduce viral replication. Researchers successfully crystallised the COVID-19 main protease (Mpro), which is a potential drug target. The Mpro in CoV is essential for the proteolytic maturation of the virus and has been examined as a potential target protein to prevent the spread of infection by inhibiting the cleavage of the viral polyprotein. The present study aimed to assess bioactive compounds found in medicinal plants as potential COVID-19 Mpro inhibitors, using a molecular docking study.

Dosage

250-500mg liposomal curcumin

Up to 2 grams standard

OREGANO

Oregano is a widely-used herb belonging to the mint family. The oil extracted from oregano leaves has a long history of medicinal uses and has been traditionally used to treat respiratory disorders such as asthma, coughs and bronchitis for many years.

Mechanism of Action in Immune Function

Oregano is rich in antioxidants due to a high content of phenolic acids and flavonoids and helps to fight the damage from free radicals. It has also shown antibacterial, antifungal and anti-inflammatory qualities.

Viral Infections[1-6]

To date, there have been a number of studies that have looked at the health benefits of oregano in relation to viral infection. In particular, carvacrol and thymol are two compounds that have been associated with antiviral properties.

One study demonstrated that participants with URTIs, who used a throat spray containing oregano oil, experienced reduced hoarseness, sore throat and coughing and had significant and immediate improvement in symptoms.

In a further study, researchers investigated the antiviral activity of oregano oil and found that it inhibited both human and animal viruses *in vitro*. Carvacrol alone exhibited high antiviral activity against the human rotavirus.

In an animal study, the antiviral efficacy of oregano oil and its primary active component, carvacrol, was investigated against the nonenveloped murine norovirus (MNV), and was found to be effective in inactivating MNV within one hour of exposure, by acting directly on the viral capsid and subsequently the RNA.

Oregano essential oil has also exhibited strong antiviral activity against several nonenveloped RNA and DNA viruses such as adenovirus type 3, poliovirus, and coxsackievirus B1.

Oregano has also shown beneficial effects on CVD and Metabolic Syndrome.

Dosage

50mg 2 x daily

N-ACETYLCYSTEINE[1]

Acetylcysteine is a derivative of the amino acid cysteine, which is required for the production of glutathione. As glutathione is the body's most powerful antioxidant, N-acetylcysteine (NAC) is valued primarily for its antioxidant role in the body. NAC was introduced in the 1960s as a mucolytic drug for chronic respiratory diseases. In hospital settings, it is also used in nebulized format in patients with acute bronchopulmonary disease (pneumonia, bronchitis, tracheobronchitis).

Cruciferous vegetables, such as cabbage, Brussels sprouts, broccoli and kale, are rich sources of sulphur-containing compounds, important in the production of cysteine. Cysteine is also found in most high-protein foods, such as poultry, yoghurt, eggs, dairy, sunflower seeds and legumes.

Mechanism of Action in Immune Function[1-8]

Cysteine helps to assist important biological functions by bonding with the amino acid glutamine to create the most powerful antioxidant known to the body - glutathione. Common threats to glutathione levels include ageing, medications, poor nutrition, stress and infections. Glutathione helps in the neutralisation of free radicals that cause damage to cells and tissues at the molecular level. Research on certain diseases associated with NAC and glutathione deficiency suggests that immune function might be improved and potentially restored by supplementing with NAC. Furthermore, studies have demonstrated that supplementing with NAC resulted in a significant increase in immune function, and an almost complete restoration of NK cells. It has also been shown to reduce the formation of proinflammatory cytokines, such as IL-9 and TNF-α.

Glutathione exhibits vasodilator properties by increasing cyclic GMP levels and by contributing to the regeneration of endothelial-derived relaxing factor. One study showed that 600 mg of NAC twice a day significantly improved lung function and symptoms in those with COPD and a 2015 meta-analysis evaluating 13 studies concluded that 1,200 milligrams of NAC per day reduced the incidence and severity of flares in people with COPD compared to a placebo.

By thinning mucus in the bronchial tubes and boosting glutathione levels, NAC may help decrease the severity and frequency of wheezing, coughing and respiratory attacks. In addition, cysteine derivatives act by breaking disulphide bridges between macromolecules, which leads to a reduction in mucus viscosity.

At higher doses (≥1200mg), NAC acts as an antioxidant through complex mechanisms, which can combat conditions of oxidative stress. Its antioxidant activity is also key for addressing numerous other conditions caused by oxidative stress, such as heart disease and pulmonary disease, all of which have been identified as increasing the severity of viral infection.

COVID-19 and other Viral Infections[1, 9-16]

It is worth noting that most research into NAC supplementation has taken place on a small scale. NAC promotes glutathione production, which has been shown to be protective in mice infected with influenza. This activity is thought to be the basis for the protective effect of NAC administration in both influenza patients and in mouse models of the disease. In human studies, a randomised double-blind trial was carried out on a total of 262 elderly subjects who received 600 mg NAC twice daily, as opposed to those receiving placebo. The group that received NAC experienced fewer influenza-like symptoms and days of bed confinement.

Results from another study showed that high levels of NAC may also suppress HIV-1 reproduction. Similarly, other research has indicated that in immune-compromised situations such as the flu, NAC may hamper the virus's ability to replicate, potentially reducing the symptoms and lifespan of the illness. It is the potential antioxidant mechanism of NAC that has generated interest with the current COVID-19 pandemic. In a preprint, patients with COVID-19 had a clear increase of glutathione reductase levels, occurring in around 40% of patients.

Several studies have researched the anti-viral activity of NAC against influenza A strains. Both *in vitro* and *in vivo* experiments show that NAC enhances glutathione levels, which reduce viral load by inhibiting viral replication in a number of viruses e.g. influenza A (H3N2 and H5N1). Preclinical data also suggests that NAC and its antioxidant properties may have purpose for use in the therapy and/or prevention of acute viral respiratory infections including influenza. NAC has also been suggested as a supportive treatment for influenza pneumonia. As reactive oxygen species play a crucial role in inflammatory responses and viral replication, antioxidants that exert antiviral and anti-inflammatory effects have been suggested as candidates for the treatment of a cytokine storm induced by severe influenza. NAC was shown to inhibit both H5N1 replication and H5N1-induced production of pro-inflammatory molecules (e.g., IL6, CCL5, CXCL8, and CXCL10) in lung epithelial cells.

Glutathione levels decrease with age, and as a result of certain disease states e.g. Type 2 Diabetes and CVD. These disease states should be supported, particularly in the case of viral assault. Low levels of glutathione are virtually universal among patients with chronic disease.

Dosage

The accepted daily supplement recommendation is 500–1,000mg

1/3 1/6 BETA GLUCANS[1]

Beta glucans are naturally occurring polysaccharides found in the cell walls of fungi, bacteria, cereals, certain mushrooms and algae. They are well-known for their ability to activate and prime the immune system. In a time before fungicides were routinely sprayed on to crops, almost everything we ate would have had yeasts, fungi or moulds present, and this was ironically, one of the key factors that kept our innate system primed and working optimally. These micro-organisms have always been a threat to us, and so the innate immune system, long ago, developed the ability to recognise beta glucans and react to them by mounting an immune response.

Mechanism of Action in Immune Function[2-4]

Beta glucans are not synthesised by the human body and therefore are recognised as non-self (e.g. viruses, bacteria, fungi, etc). The innate immune system identifies them as a potential pathogen, although they themselves do not possess the ability to cause an infection. The recognition of these specific molecules triggers the upregulation of the immune system.

Beta glucans are known to modulate immune activity, mostly by priming or training innate immune responses through interactions with pattern recognition receptors (PRRs). Innate immune training refers to a newly recognized phenomenon wherein compounds may "train" innate immune cells, such that monocyte and macrophage precursor biology is altered to mount a more effective immunological response.

Innate immune cells do not have the ability to recognise a wide range of antigens, however they carry on their surface an extremely important group of receptors called Toll-Like Receptors (TLRs). TLRs only respond to a limited number of compounds, but as these compounds are basic elements that occur in every bacterium and virus, they are able to recognise almost any infection and initiate an immune response. When they recognise a fungal wall compound such as a beta glucan, for example, they initiate an antimicrobial response involving heightened macrophage and dendritic cell activity.

When the TLRs are exposed to viral DNA they elicit a different antiviral response. All innate immune cells have CR3 receptors, which specifically recognise beta glucan. Beta glucans are therefore, able to stimulate the body's own antibiotic reaction because the 1-3 particle exactly fits to the C3 receptor. After ingestion, beta glucans are taken up by macrophages in the gut associated lymphoid tissue (GALT) and are phagocytosed (eaten). Macrophages digest the beta glucans into smaller fragments and release them over time, into the bloodstream. The fragments bind to receptors on neutrophil granulocytes and NK cells, priming them and making them more active. Neutrophils are involved in killing bacteria, and the NK cells destroy both virally infected cells, leading to an increased resistance to infection and enhanced apoptosis of abnormal cells.

Beta glucans can also evoke a response via the acquired immune system. When innate dendritic cells are activated, they communicate the presence of a pathogen to the acquired immune system, warning that an infection is likely. This instructs naïve T- helper cells to develop into TH1 cells, which have anti-microbial properties, rather than TH2 cells, which are involved in allergic reactions. The resulting increase in the TH1/TH2 ratio has important anti-allergy effects.

COVID-19 and other Viral Infections[1, 5-15]

Beta glucans' ability to activate macrophages and prime neutrophils has been extensively tested in over 800 studies. Many human studies have demonstrated that beta glucans can decrease the symptoms associated with cold and flu and URTIs compared to placebo. For example, a study in healthy subjects showed a 20-25% reduction in common cold episodes with supplementation of yeast beta glucan 1-3, 1-6. It concluded that the beta glucan preparation increased the body's potential to defend against invading pathogens. Another study looking at 49 adults aged 50 to 70 showed that daily oral *β*-1-3, 1-6 glucan may protect against URTI's and reduce the duration of URTI symptoms in older individuals once infected. Furthermore, beta glucan supplementation maintained immune function in endurance athletes and has been shown to reduce post-exercise URTIs in marathon runners.

In an animal study, a high proportion of test rodents who received beta glucan preventatively, seven days before exposure to influenza survived. In addition, a study carried out on pigs showed that beta glucan reduced the harm to the lungs after infection with swine flu virus, and reduced replication of the virus itself. Many other studies support the use of beta glucans in promoting viral eradication or inactivation.

It is well-known that there are increasing problems with antibiotic and anti-viral resistance. Priming the innate immune system with 1-3, 1-6 beta glucan has repeatedly been shown to increase resistance to bacteria and viruses in humans, fish, poultry, Guinea pigs, pigs and honey bees.

Therapeutic Dose

Studies have demonstrated positive immunomodulatory effects using doses between 50-500mg, with doses between 100-500mg showing greatest effect. Other studies have suggested 5mg/kg/day as a preventative dose and 10mg/kg/day therapeutically.

Ancestral diets were rich in 1/3 1/6 beta glucans, but modern-day diets are naturally low in these polysaccharides.

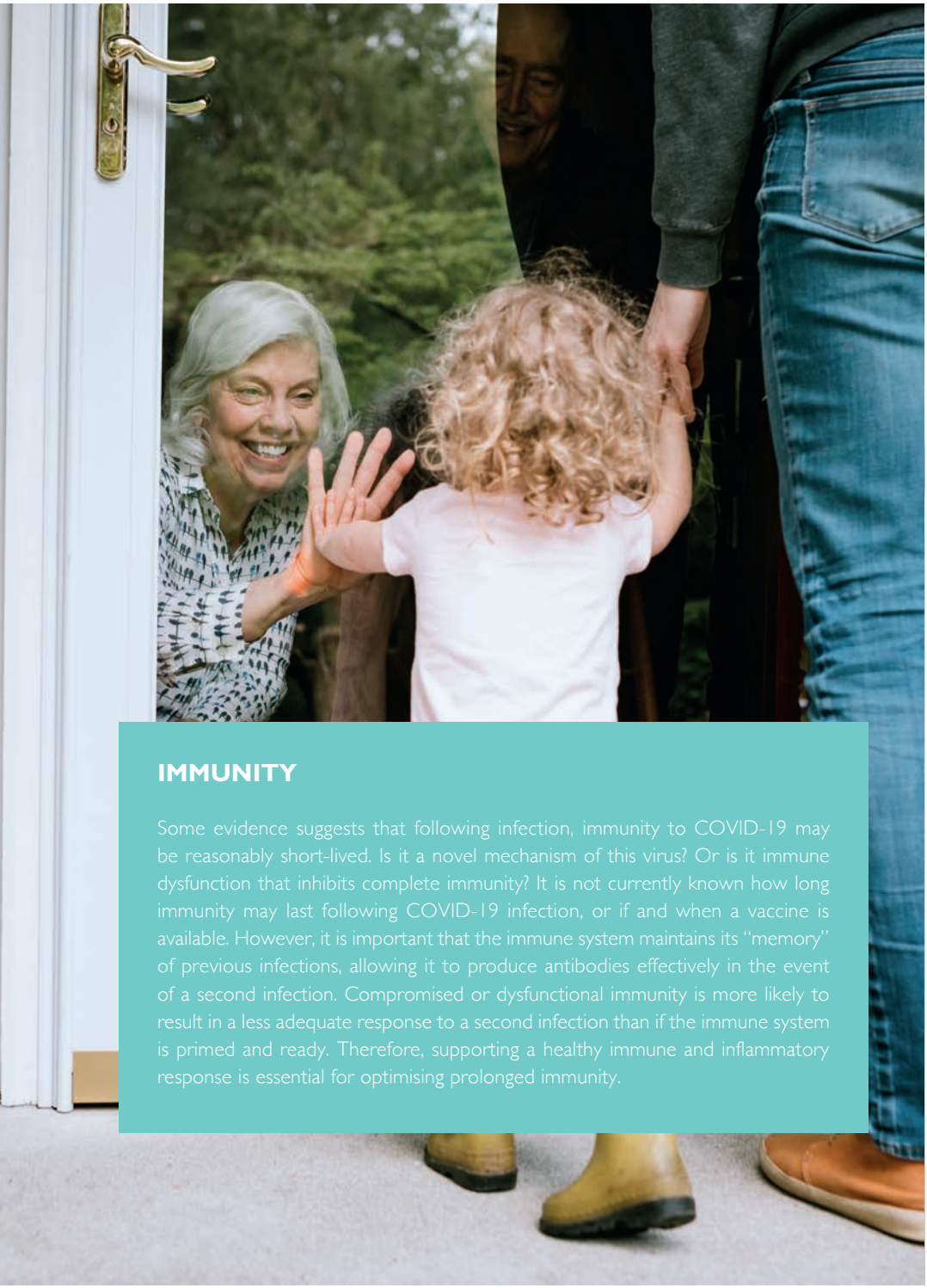
CYTOKINE STORM[1-4]

Cytokines are inflammatory immunologic proteins that are there to fight off infection. It has been well-documented that the severity of COVID-19 is often due to a cytokine storm, where inflammation runs out of control and the body's own inflammatory response becomes more dangerous than the infection itself. The main problems are therefore not brought about by the virus itself, but by the extreme immunological response to the infected organs.

SARS-CoV2 has been shown to activate the NLRP3 inflammasome, which is strongly involved in the hyper-activation of the innate immune response and the uncontrollable release of pro-inflammatory cytokines. The body requires an appropriate inflammatory response to react to initial infection and signals to other parts of the immune system to begin the fight against the infection. Promoting an appropriate inflammatory response is therefore, essential. Many people already have heightened inflammation as it is a driver of many chronic conditions (CVD, autoimmune disorders, dementia, diabetes type 2 etc) - this may account for the increased risk of a severe infection due to comorbidities. Many suggested interventions are to normalise the inflammatory response to help support resilience and help to prevent activation of the NLRP3 inflammasome.

DHA/EPA

In addition to the nutrients mentioned - omega-3 fatty acids help to regulate inflammation and are also likely deficient in a typically Western diet. Omega-3 has been shown to reduce inflammatory cytokines and there have been some trials using omega-3 in response to ARDS. Increasing the ratio of omega-3 to omega-6 can help move away from a hyper-inflammatory response to infection. The omega-3 fatty acids, EPA and DHA present at the site of inflammation are enzymatically converted to specialized pro-resolving mediators known as resolvins, protectins, and maresins. These molecules work together to orchestrate the resolution of inflammation and to aid healing, including in the respiratory tract. Notably, nutritional deficiencies in these essential fatty acids can result in delayed or suboptimal resolution of inflammation. This could be crucial in the context of severe COVID-19 which presents as uncontrolled inflammation.



IMMUNITY

Some evidence suggests that following infection, immunity to COVID-19 may be reasonably short-lived. Is it a novel mechanism of this virus? Or is it immune dysfunction that inhibits complete immunity? It is not currently known how long immunity may last following COVID-19 infection, or if and when a vaccine is available. However, it is important that the immune system maintains its "memory" of previous infections, allowing it to produce antibodies effectively in the event of a second infection. Compromised or dysfunctional immunity is more likely to result in a less adequate response to a second infection than if the immune system is primed and ready. Therefore, supporting a healthy immune and inflammatory response is essential for optimising prolonged immunity.

STEP 2.
GUT HEALTH AND IMMUNITY[1-5]

Nutrition plays a vital role in determining the composition of the gut microflora and the gut microflora equally has an important role to play in their interactions with the immune system, and subsequently in health and disease. Supporting a diverse microbiome is a vital part of immune health.

The gut microflora has a strong influence on the production of serotonin within the gut and therefore, on the stimulation of the vagus nerve. Research suggests that commensal bacteria within the gut stimulates the host intestinal cells to produce serotonin. Supporting the balance of the gut microflora is therefore, so important for serotonin production and the maintenance of a stable mood.

Gut dysbiosis refers to an imbalance of microorganisms and can lead to intestinal permeability or 'leaky gut'. This allows toxins to enter the bloodstream, which can evoke an immune response and essentially dysregulate the immune system and cause inflammation. Persistent immune activation, over time, can cause problems with immunity and can also set the stage for disease. The potential role of the intestinal microbiota in the context of disease is well documented. It also has implications for the innate immune system in the context of viral infection.

Mechanism of Action in Immune Function[1-3]

The respiratory tract microbiota influences the host immune response to viruses. Acute respiratory viral infections can disrupt the host-microbiota interactions and create intestinal dysbiosis through the post-viral immune responses that contribute to pneumonia development by the secondary bacterial infection. The diverse intestinal and respiratory tract microbiota is therefore a critical determinant for supporting immunity. Probiotics are live microorganisms and have been shown to promote a healthy balance of gut bacteria. The mechanisms of action with regard to probiotics and their effect on the microbiota include:

- Modulating composition and/or activity of host microbiota
- Enhancing epithelial barrier integrity
- Modulating the host immune system
- Adhering to the mucosa and epithelium, inhibiting pathogen adhesion and/or growth
- Inhibiting pathogen virulence factor expression

COVID-19 and other Viral Infections[1-9]

Interferons are the first line of immune defence against viral infection and are probably the critical antiviral cytokines in the respiratory epithelial surfaces during the early stages of viral infection. Research has shown that certain strains of *Lactobacillus* influence the interferon responses following influenza infection.

Several studies have demonstrated that respiratory infections are associated with a change in the composition of the gut microbiota. The gut microbiota has been shown to affect pulmonary health through a vital cross-talk between the gut microbiota and the lungs, which is referred to as the "gut-lung axis." The gut-lung axis is bidirectional, meaning that endotoxins and microbial metabolites can impact the lung through the blood and when inflammation occurs in the lung, it can affect the gut microbiota as well.

The composition of a balanced gut microbiota is known to have a major influence on the effectiveness of lung immunity. Recently, it has been shown that there are increased amounts of pathogenic gut bacteria like Bacteroides and Enterobacter in the lungs of ARDS patients. These bacteria are not normally present in the lung, and likely got there by a process called translocation, whereby the intestine becomes more permeable and allows gut bacteria into the bloodstream. This translocation causes a significant inflammatory response by the body. A current area of interest is the role that these bacteria are playing in the excessive inflammatory response and ongoing lung damage in ARDS.

Gut microbiota diversity decreases as we age and COVID-19 has been predominantly fatal in elderly patients. One of the serious clinical manifestations of COVID-19 is pneumonia and progression to ARDS, especially in elderly, immune-compromised patients. Numerous experimental and clinical observations have suggested that the gut microbiota plays a key role in the pathogenesis of sepsis and ARDS. A healthy gut microbiome essentially could be pivotal therefore, in maintaining an optimal immune system to prevent an array of excessive immune reactions that eventually become detrimental to lungs and vital organ systems.

Notably, one recent Chinese study did examine probiotics' potential in preventing secondary bacterial infection, specifically in COVID-19 patients. The researchers speculated that targeting gut microbiota may be a new therapeutic option or at least an adjuvant therapeutic choice.

In animal studies, germ free mice, devoid of their intestinal microbiota, were shown to have impaired pathogen clearance capability in the lung. Furthermore, in other murine models, removal of certain gut bacteria by antibiotics led to an increased susceptibility to influenza virus infection in the lungs.

Another study demonstrated that a strain of *L. plantarum* was associated with a reduced incidence of URTI after one to two months, and reduced nasal symptoms after three months. Further to this the severity and duration of URTI in another study was reduced in people

consuming a combination of *L. gasseri*, *B. longum* and *B. bifidum*. Research has also demonstrated that children consuming *B. lactis* and *L. acidophilus* had less severe and shorter duration of cold and flu-like symptoms.

In a 2007 study carried out on children with acute gastroenteritis, the administration of *S. boulardii* resulted in significant increases in CD8 lymphocytes, serum immunoglobulin A and decreases in C-reactive protein levels, suggesting that *S. boulardii* treatment enhances the immune response.

Alterations of gut microbiota have also been associated with various diseases like type 2 diabetes and CVD.

Consider Supporting a Healthy Bowel Flora by:[1,2]

- Consuming fermented foods such as kefir, kombucha, sauerkraut and miso – all this down-time is a great opportunity to experiment with some fermenting
- Consuming prebiotic (fuel for gut bacteria) foods and polyphenols from chicory, olives, baked apples and Jerusalem artichoke
- Taking a live bacteria supplement

STEP 3.
IMMUNITY AND SLEEP[1,2]

Healthy sleep is essential for normal immune function, however, for some people a good night's sleep can completely evade them. This can become a vicious cycle of increased anxiety and reduced activity, leading to further reduced sleep quality.

Lack of sleep can weaken immunity, thus increasing susceptibility to infection.

Poor sleep has been shown to:

- Impair proliferation of lymphocytes
- Decrease HLA-DR expression (involved in antigen presentation to T-cells and therefore important for a T-cell response)
- Upregulate CD14+ (important aspect of the immune system but associated with inflammatory conditions)
- Cause variations in CD4+ and CD8+ T lymphocytes
- Increase or disrupt steroid hormones, such as cortisol, which can then have a negative effect on sleep

Additionally, sleep patterns are altered during the immune response, suggesting that sleep and the immune response are linked through bidirectional communication. During sleep, important processes occur with regard to endocrine function - for example, rises in the level of hormones such as prolactin and growth hormone (which both have stimulatory effects on immunity). Sleep also inhibits cortisol, which can have an inhibitory effect on immunity.

Sleep, therefore, promotes immune function via hormonal control. The endocrine milieu during early sleep critically supports:

- The interaction between antigen presenting cells (APC) and T cells, as evidenced by an enhanced production of IL-12
- A shift of the Th1/Th2 cytokine balance towards Th1 cytokines
- An increase in Th cell proliferation
- It is also likely to facilitate the migration of naïve T cells to lymph nodes

Additionally, without sufficient sleep, your body makes fewer cytokines (a type of protein that targets infection and inflammation). Cytokines are both produced and released during sleep, causing a double whammy if you skimp on shut-eye. Remember, we need an inflammatory response to infection, but it must be appropriate and not extreme.

HOW DO WE SLEEP?[1-5]

Throughout the day we are exposed to daylight and during this time the brain signals the production of serotonin (our "feel good" neurotransmitter). When the sun goes down, the pineal gland recognizes the reduction in light and signals the conversion of serotonin to melatonin. Melatonin is a neurotransmitter, which is responsible for instigating sleep.

Our circadian rhythm is also governed by the relationship between melatonin and cortisol. Cortisol is a hormone that is essential for our sleep/wake cycle and is also released during periods of stress. It is important for waking us up, therefore it is high in the morning and begins to drop during the day to its lowest level in the evening, which allows us to sleep. Cortisol inhibits melatonin; therefore, this drop in the evening is essential for allowing sleep to occur. During periods of stress, cortisol levels can remain high in the evening and can significantly affect the ability to fall asleep. Many people who are stressed can feel tired all day and then wake up in the evenings, leading to poor sleep, which can further exacerbate stress.

Insulin (released after carbohydrate consumption) can also inhibit melatonin, therefore it is recommended not to eat a large meal 3 hours before bedtime.

Another important neurotransmitter is GABA. GABA is the main inhibitory neurotransmitter of the central nervous system and is responsible for relaxation and calm. It is well established that the activation of GABA receptors favours sleep. It has been shown that people who suffer from insomnia have lower levels of GABA.

SUPPORTING HEALTHY SLEEP

When clients present with sleep disturbances, it is important to consider the role of hormonal regulation. Conditions including insulin resistance, oestrogen dominance, reduced testosterone, adrenal and thyroid dysfunction should all be considered, as well as other factors independent of hormone balance.

Nutrients such as tryptophan, magnesium, vitamin B6, glycine, L-theanine and natural sources of melatonin can support restful sleep. Sleep can be promoted either by inhibiting wake-promoting mechanisms or by increasing sleep promoting factors through nutritional interventions. Based on one review of the existing scientific literature, there appears to be considerable scope for further investigation of nutrition interventions designed to enhance sleep quality.

Healthy Sleep: Good Habits and Tips

Create a sleep ritual – this can be a set of little things to do before bed to help prepare physically and psychologically for sleep and can guide the body into a deep, healing sleep. It may take weeks or months, but using these tools in a co-ordinated way, along with addressing any relevant hormone imbalances, will eventually reset biological rhythms.

- Optimize exposure to natural light during the day
- Have time before bed in natural dimming light, away from bright screens
- Sleep in darkness and ensure it is quiet – consider using a sleep mask or earplugs
- Consider using a low wattage incandescent bulb
- Keep a regular sleep cycle
- Set a regular bedtime routine – go to bed at the same time each night. Choose a time when you are generally feeling tired each night. Try not to break the routine
- Wake up at the same time each day, even at weekends. If you are getting enough sleep you should wake naturally without an alarm. If you need an alarm clock then you should go to bed earlier
- Nap to make up for lost sleep during the day if possible, rather than disturb the normal sleep/wake cycle

- Fight after dinner drowsiness, otherwise napping at this time could result in waking through the night
- Consider an earlier meal and a walk after eating
- Create a relaxing bedtime ritual

Making a consistent effort to relax and unwind before bed will allow for an easier and deeper sleep. A peaceful bedtime routine sends a powerful signal to the brain that it is time to wind down and let go of the day's stresses.

- Keep noises down (earplugs might help)
- Keep the room cool - most people sleep best at around 18°C, with adequate ventilation
- Make sure the bed is comfortable - waking with a sore back or neck suggests the mattress or pillow may need changing
- Create an aesthetic environment that encourages sleep – use serene and restful colours and eliminate clutter and distraction
- Avoid work or watching television in bed
- Consider using a relaxation, meditation or guided imagery CD - any of these may help with getting to sleep and will certainly help with relaxation
- Eat well and try and get regular exercise/physical activity
- Eat at least 3 hours before bedtime by making dinnertime early in the evening. Fatty, spicy, rich or heavy foods are best avoided in the evening
- Avoid alcohol before bedtime - it may help to initiate sleep but can cause interruptions and poor quality of sleep
- Cut down on caffeine - ideally try not to consume caffeine after midday. Some people take 12 hours to metabolise caffeine. Be mindful of any medications that may contain caffeine, such as headache tablets and other painkillers, for example. Some prescriptions may contain caffeine, so always discuss with your GP before making changes to any medication
- Avoid too many liquids in the evening, as this may cause middle of the night waking to eliminate

- Quit Smoking - smoking causes sleep problems in numerous ways. Nicotine is a stimulant, plus smokers can experience nicotine withdrawal during the night, making it harder to sleep

- Avoid high intensity exercise after dinner

Supplements to Consider

- **5-hydroxytryptophan (5HTP)** – is a precursor to serotonin and can be useful for initiating sleep for some people, particularly if melatonin or serotonin levels are low

- **Montmorency Cherry** - a natural source of melatonin, the neurotransmitter responsible for the induction of sleep

- **L-theanine** - has been shown to aid relaxation and reduce anxiety by increasing alpha brain waves and GABA levels (the calming brain neurotransmitter)

- **Magnesium** – a cofactor for melatonin production; it also supports muscle relaxation

STEP 4.
IMMUNITY AND STRESS[1-6]

Chronic stress has been associated with the suppression of the immune system and there are many studies that have shown an association between stress and reduced immune function. One study looked at students at the beginning of term, and then during exam time, and found that there was a reduction of B lymphocytes, an essential part of immunity during periods of increased stress.

The relationship between stress and immunity is complex. It has been shown that prolonged levels of the stress hormone cortisol can lead to both a decreased resistance to infection, and also an over-activation of immune function and inflammation, potentially leading to auto-immune conditions. Supporting a healthy stress response and adrenal function is therefore, essential for maintaining immune homeostasis.

Psychological or physiological stress causes the adrenal glands to release adrenaline, which provides energy and boosts immune function over a short period. At the same time, the body also releases cortisol – a hormone which lowers immune function. As soon as the stress subsides, adrenaline stops pumping so readily, leading to a temporary surplus of cortisol, which can weaken the immune system. It is this vulnerable state that can leave people more susceptible to illness.

When supporting immune function, it is important to look at the health of the adrenal (stress) glands.

NUTRIENTS THAT ARE IMPORTANT FOR A HEALTHY STRESS RESPONSE INCLUDE:

- **Vitamins C, B5 and B6** – these collectively support normal adrenal function and cortisol production
- **Magnesium** – an essential cofactor for many enzymes involved in the production of adrenal hormones and therefore depleted in times of stress; it is also a muscle relaxant of both skeletal and smooth muscle
- **Phosphatidyl serine** – has inhibitory effects on the HPA (stress) axis and has been shown to lower cortisol levels
- **Adaptogenic herbs** – Ashwagandha, Siberian ginseng, Panex ginseng, liquorice and Rhodiola may be useful in modulating the stress response

LIFESTYLE

Many lifestyle factors can help to reduce cortisol levels and calm the mind and body, here are a few examples:

- Meditation or mindfulness
- Moderate, enjoyable exercise
- Yoga
- Reading

Additionally, stress can contribute to low mood and poor sleep, therefore these need to be supported as well. Please see sections 3 and 5 to read further about stress in relation to exercise and sleep.

STEP 5.
IMMUNITY AND EXERCISE[1]

Exercise has a significant effect on the immune system. However, exercising too much can be just as bad as not exercising at all, when it comes to immunity.

Dr James Levine is the co-director of the Mayo Clinic and the Arizona State University Obesity Initiative. He is also the author of the book 'Get Up! Why Your Chair Is Killing You and What You Can Do About It.' In 2014, he summed up his findings after many years of studying the adverse effects of our increasingly sedentary lifestyles. He stated that "sitting is more dangerous than smoking."

His investigations show that blood sugar levels, blood pressure and cholesterol rise as a consequence of sitting for long periods, which has a negative impact on the immune system.

Those with diabetes are more susceptible to infections as high blood sugar levels can weaken immune system defences. A weaker immune system is one potential reason people with high blood pressure and other health problems are at an increased risk for viruses. A weak immune system is less able to fight viral assault.

Hypercholesterolaemia leads to cholesterol accumulation in macrophages and other immune cells, which promotes amplification of inflammatory responses. Although cholesterol accumulation, through the promotion of inflammatory responses, may have beneficial effects in the response to infections, it can exacerbate diseases that are associated with chronic metabolic inflammation, including atherosclerosis and obesity.

The solution to these adverse events does not involve a prescription but includes a moderate amount of movement, and avoidance of a sedentary lifestyle.

Exercise immunology is considered a reasonably new area of scientific research with 90% of papers published in the last 30 years. The immune system is very responsive to exercise, and it can be influenced either negatively or positively depending on the extent and duration of physiological stress imposed by the workout. These effects will be discussed below.

POSITIVE EFFECTS OF EXERCISE ON THE IMMUNE SYSTEM[1-7]

Immunosurveillance, is a term used to describe the processes by which cells of the immune system look for, and recognise foreign pathogens, such as bacteria and viruses.

It has been consistently shown that acute exercise sessions, of less than 60 minutes, can enhance immunosurveillance. To explain this in more detail - during moderate and vigorous-intensity aerobic exercise bouts of less than 60 minutes, the antipathogenic activity of tissue macrophages occurs in parallel with an enhanced recirculation of immunoglobulins (antibodies), anti-inflammatory cytokines, neutrophils, NK cells, cytotoxic T cells (which play a major role in host defence against viral infection), and immature B cells. All of these play critical roles in immune defence activity and metabolic health.

Those who exercise regularly report fewer URTIs than their sedentary peers. Data from 3 randomised studies showed that daily physical activity reduced the number of days with sickness. In one study, women in the exercise groups walked briskly 35–45 minutes, 5 days per week for 12–15 weeks, while the control groups remained physically inactive. It was found that walkers experienced about half the days with URTI symptoms than those of the sedentary controls. However, these studies failed to demonstrate that immune function, measured in the resting state, is altered after 12–15 weeks of near-daily moderate physical activity. For these reasons, it has been hypothesised that the acute immune changes that occur during, and shortly after the moderate exercise bout itself may explain the lowered risk of URTI. In other words, host protection against pathogens is improved through a summation effect of improved immunosurveillance that occurs acutely with each moderate exercise bout and therefore transient.

STRESS, EXERCISE AND THE IMMUNE SYSTEM[1,2]

Stress can inhibit many critical functions of the immune system and reduce the ability of immune cells to do their job. Immune cells seek out vulnerable areas in the body and prevent viruses and pathogens from gaining a foothold. A well-functioning immune system reduces the impact of viral infection and can reduce recovery time too.

Exercise can be an effective component of a stress management programme and can increase the production of β-endorphin - the body's natural pain killer. Exercise and stress research have predominantly focused on aerobic exercise and there has been consistent findings that people report feeling calmer after a 20-30-minute session - the calming effect can last for several hours after. Human research indicates that being physically active improves the way the body handles stress, due to changes in hormone responses. Exercise affects neurotransmitters

in the brain, such as dopamine and serotonin which affect our mood and behaviour. In addition to the physiological mechanisms, it is also likely that exercise provides a break from the source of stress itself.

DIABETES AND THE IMMUNE SYSTEM[1-3]

Diabetes UK reported that in May 2020, one in four people (26%) who died in hospital in England following a diagnosis of coronavirus, also had diabetes. This new data shows us that of the 23,804 deaths recorded in the study, 7,466 (31.3%) had type 2 diabetes, 365 (1.5%) had type 1 and 69 (0.3%) had other types. Researchers further commented that it is important to remember that about 90% of people with diabetes have type 2 and that the majority of these people are aged 60 years old or over. It is known that age is strongly linked to coronavirus mortality. Overall, there have been more deaths recorded in people with type 2 diabetes. However, Diabetes UK have also stated that when looked at proportionally – and taking into account differences between people such as age, sex and ethnicity – even though there were fewer deaths in type 1 diabetes, the condition itself is linked with a higher risk. People with type 1 diabetes were found to be 3.5 times more likely to die from coronavirus in hospital, and people with type 2 diabetes twice as likely than people without diabetes.

How does this relate to movement and exercise? Mechanistic studies in humans suggest that moderate acute elevations in interleukin 6 (IL-6), as provoked by exercise, exert direct anti-inflammatory effects by an inhibition of tumour necrosis factor alpha (TNF-α) and by stimulating IL-1ra (IL-1 receptor antagonist), thereby limiting IL-1β signalling. In addition, IL-6 has a direct impact on glucose and lipid metabolism. Moreover, indirect anti-inflammatory effects of exercise may be mediated via improvements in body composition, for example. Physical activity therefore, represents a natural strong anti-inflammatory and metabolism-improving strategy with minor side effects.

Additionally, acute and chronic exercise-induced immune changes are now being described as important mechanistic pathways for elucidating reduced cancer and heart disease risk among the physically active.

To conclude, as the positive effects of short duration, moderate exercise on the immune system has been found to be transient, movement needs to be consistent and therefore incorporated into daily lives.

EXERCISE AND THE MICROBIOME[1-3]

Gut-associated lymphoid tissue (GALT) is the prominent part of mucosal-associated lymphoid tissue (MALT) and represents almost 70% of the entire immune system. Therefore, when focussing on improving the immune system, emphasis must be placed on regulating gut microbiota composition. Studies have found that exercise may represent a strong modulator of gut microbiota composition.

Some authors have hypothesised that many of the well-known positive health effects of exercise may be mediated by its beneficial modifications on the gut microbiota.

However, when there is an excess of exercise, these beneficial effects are outweighed by increased intestinal permeability and oxidative stress, which promotes inflammation and a catabolic state that can negatively impact on the functionality of skeletal muscle.[1-6] Conversely, effects of inactivity on the muscle and vascular system may be at least partly mediated by negative changes of the gut microbiota towards dysbiosis.

In healthy subjects who regularly perform physical activity, exercise promotes healthy microbiota composition. But as stated, this equilibrium may be disrupted by sedentary lifestyle or excessive exercise, resulting in dysbiosis of the gut microbiota.

NEGATIVE EFFECTS OF PROLONGED INTENSE WORKOUTS[1-5]

The potential link between prolonged, intensive exercise and increased risk for illness has been an active area of research since the 1980s. Early epidemiologic studies indicate that athletes engaging in marathon and ultramarathon race events and/or very heavy training were at increased risk of URTIs.

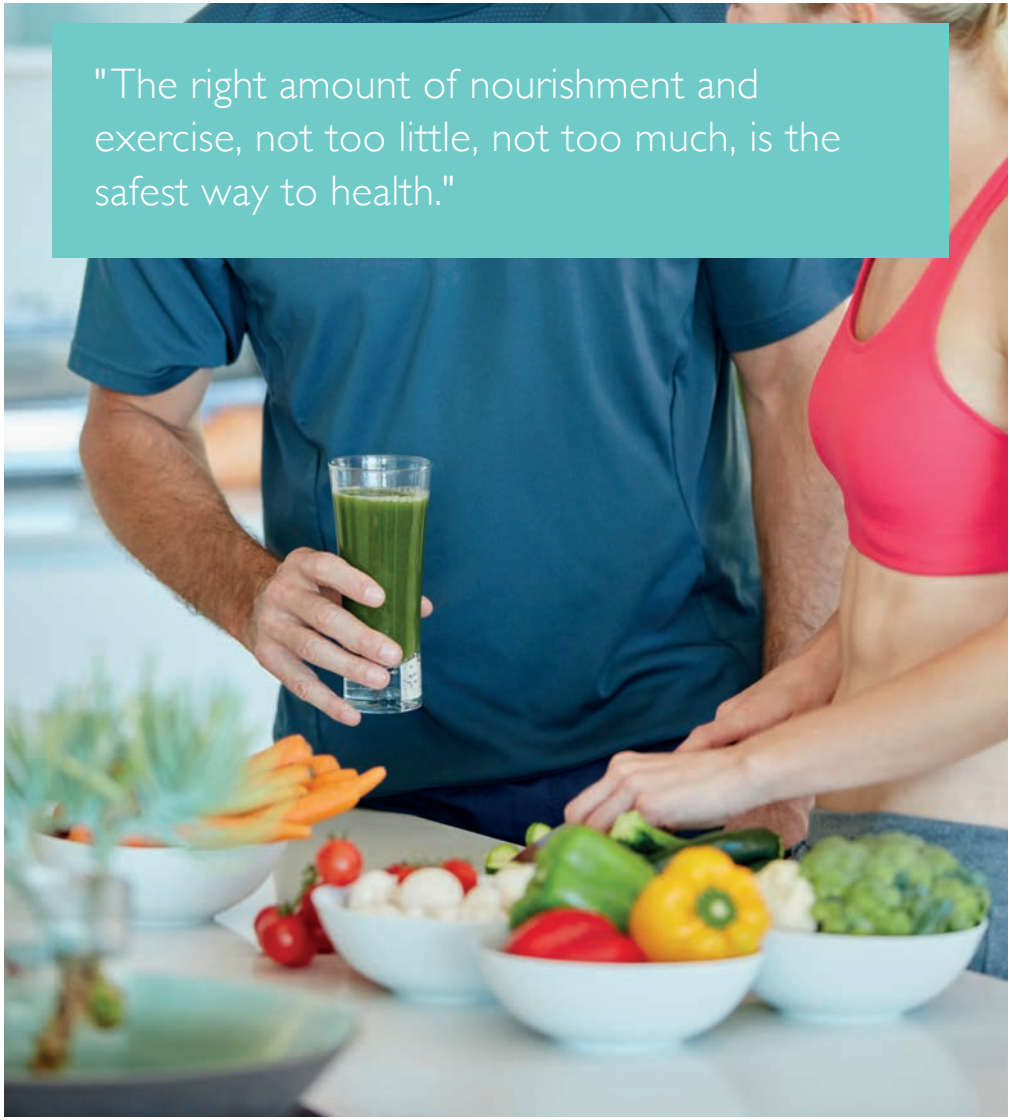
Intense training workloads, competition events, and the associated physiological, metabolic, and psychological stress are linked to immune dysfunction, inflammation, oxidative stress and muscle damage.

David Nieman is the director of the Appalachian State University Human Performance Lab. His research team have recently studied US Explorer Colin O'Brady's immune function during the adventurer's ski trek across Antarctica. Using finger prick blood drops O'Brady had collected over a 28-week period, the researchers measured immune-related proteins in his blood and noted that he had gone through an extended bout of high-intensity effort. Nieman found a dysfunctional immune response during a sustained period of mental and physical distress while trekking across the Antarctica.

Nieman has also reported that when there is a novel virus like COVID-19 and no vaccine or cure available, athletes tend to be in the vulnerable category. Athletes that are pushing themselves doing long training sessions of two or three hours are considered to be in the group of immunocompromised individuals.

The immune system is only temporarily suppressed due to strenuous exercise, so if exposed to a new virus during that time, the risk is potentially greater.

A statement written by Hippocrates 2,500 years ago sums this topic up quite nicely:



EXERCISE PRESCRIPTION

Regular exercise is one of the pillars of healthy living and as discussed above, consistent, short duration moderate exercise has been shown to be effective in boosting immunity.

Below are some exercise examples:

Indoor Activities

- Walk briskly around the house or up and down the stairs for 10-15 minutes, 1 – 3 times daily
- The NHS provide gym-free exercises www.nhs.uk/live-well/exercise/gym-free-exercises. There are also a number of 10-minute indoor workouts available via this link
- Watch an exercise video – there are many to choose from on YouTube. Try search terms such as: 15-minute beginners exercise at home; Best workout to do at home; 10-minute workouts to do at home
- Dance to your favourite music
- Use home cardio machines such as a treadmill, if you have one
- Muscle strength training can be completed outdoors in a park or your garden, or in a gym (see below for routine ideas)
- Download a strength workout app to your smart phone, such as "10-minute no equipment strength training"
- Perform Pilates or yoga – deep breathing, stretching and mindfulness may also reduce anxiety. Again, there are a number of videos available on YouTube with free or paid subscriptions
- Find ways to do simple muscle strengthening exercises around your house such as:
    - Squats or sit-to-stands from a sturdy chair
    - Push-ups against a wall, the kitchen counter or the floor
    - Lunges or single leg step-ups on stairs
- Finally, if watching TV, get up during every commercial (or periodically) and do a lap around your home or an active chore. For example, walk up and down the stairs 3 times.

Outdoor Activities

- A daily brisk walk for 35-45 minutes. If you can, try to incorporate green spaces in to your walk. You could listen to a podcast or some music whilst walking
- Join a walking group such as Ramblers www.ramblers.org.uk, www.walkingforhealth.org.uk, www.meetup.com
- Cycling – either road biking or mountain biking for at least 45 minutes, 2-3 times per week
- Gardening is not only good exercise but can be a de-stressor too
- Play outdoor active games with your family such as football or rounders
- Take your dog for a walk

Find an exercise regime that can be done in a small space and is a whole-body routine. This should take 10-20 minutes depending on how many repetitions you perform.

Marching on the Spot

A great warm up for the upper and lower body.

1. March on the spot lifting the knees up to hip height if possible. If the right knee is lifting, the opposite arm comes forward too. Attempt to increase the range of movement in the shoulders/arms.
2. Perform 10-30 repetitions (reps)

Jumping Jacks – without the jump

This is a good warm-up exercise. It will get your heart pumping and warm up the muscles. You can exaggerate the arm movements to increase the warm-up of the shoulders.

1. Start by standing hip width apart with arms down by your sides.
2. Step your right foot out to the side, and at the same time bring your arms up above your head.
3. Return to your starting position.
4. Immediately step your left foot out.

Perform 20-30 reps

Shoulder Mobilisation

This is a great way of increasing mobilisation in the shoulders and is especially useful if you have been in flexion much of the day. For example, when working at a desk, looking at your phone or driving etc.

1. Start by standing hip width apart with arms down by your sides.
2. Take both arms out in front of you so the hands are in line (at the same height) as the shoulders.
3. Squeeze the shoulders backwards so you feel the shoulder blades moving toward each other and then release back to starting position.
4. Ensure you keep the shoulders relaxed (don't let them lift up toward your ears!)
5. As time goes on, you should feel more mobilisation in this area. It is a great release for the shoulders.

Perform 10 reps then take a 5 second break and repeat.

Standing Knee Raise

This exercise should be performed slowly as this will help with co-ordination and balance. You can use a chair too if balance is an issue. This exercise works on the quadricep (thigh) muscles and the abdominals.

1. Start by standing hip width apart with arms down by your sides.

2. Lift the right knee up to hip height, no more. Attempt to pull the abdominals in slightly as you lift (this will help with stabilisation and work the abdominal muscles) and breathe out.

3. Breathe in as you lower the leg.

4. Change to the other side.

Perform 20 reps.

Side Leg Raises (or hip abductor exercise)

Hip abduction exercises are important because they strengthen the glutes (muscles in your bottom) and this in turn can help improve hip stability. In addition, if you are looking to work harder, then a loop resistance band can be placed around the calves as this will create more resistance during the exercise.

1. Start by standing hip width apart with arms down by your sides.

2. The movement will be coming from the hip area so lift the right leg out to the side, but just enough for you to feel the right glute muscles work. So, think about squeezing the glute muscles to lift your leg out to the side. If you can't feel the glutes working, you will not be performing the exercise correctly.

3. Perform the same exercise on the left side.

Perform 10 reps, rest for 5 seconds. Repeat 2-3 times.

Squats

Squats help to build strength in the body. Leg muscles worked are quadriceps, hamstrings and calves. This exercise promotes whole body muscle building, improving muscle mass.

However, squats are difficult to perform correctly and if executed incorrectly can put additional stress on ligaments and joints, increasing risk of injury. You may wish to watch a video or get an exercise professional to check your form.

1. Find a foot stance that feels best for you. Pointing your toes slightly outwards helps, but keeping them parallel is fine, too. If you're not sure what is best, start by putting your feet shoulder-width apart and pointed about 15 degrees outwards.

2. Now focus on squeezing your knees slightly outwards and slightly pull the abdominals in (keep them contracted throughout).

3. Look straight ahead, breathe out and as you start to bend your knees, ensure you put the weight into your heels and move your bottom backwards. Don't just bend your knees. If you are doing the exercise correctly, you should feel the glute muscles working.

4. Don't allow your knees to move towards each other.

5. Keep your knees roughly in line with your toes.

6. Don't forget about your upper body – look straight ahead and don't allow your back to round.

7. Keep the weight into the heels and you squat and come back to standing, breathing in, and repeat.

So, lots to think about!

Perform 10 reps, rest for 10 seconds and repeat 1-3 times.

Half Plank

This is a great exercise that works the deep abdominal muscles which support the spine.

1. Begin by lying on your front.
2. Come up onto your elbows. Ensure the shoulders are placed in line with your elbows.
3. Concentrate on keeping the shoulders relaxed and as you breathe out, squeeze and lift just your abdominal muscles.
4. Once you have tried this a few times and can feel the abdominals working, you can progress to the half plank.
5. Now, when you lift your abdominal muscles away from the mat/floor, focus on trying to lift your hips/back but ensure that you are using your abdominal muscles to lift you.
6. Hold the lift for a few seconds and release.
7. Note that the knees can stay down on the mat/floor.
8. Keep breathing throughout the exercise – don't hold your breath.
9. Ensure your back is not dipping, so should look flat when you are in the lifted position.
10. If you would like to increase the intensity of the exercise, change your starting position so that the elbows are slightly forward from the shoulders and on each exercise, you could move the elbows further forwards. You will notice the difference in intensity!

Perform 3-5 reps holding the position for 5 seconds, take a rest for 10 seconds and perform 3-5 reps again.

STEP 6.
KEEPING YOUR HOME HEALTHY – TOXINS IN THE HOME

We are exposed to many toxins and environmental pollutants during our lives and many of these can come from within our home. This can contribute to inflammation and has been shown to have a detrimental effect on our health, including our mood. As we are currently spending more time indoors it can be helpful to consider the sources of toxins in the home to help reduce exposure.

MOULDS[1–3]

Inhaling mould fragments or spores can inflame the airways, causing nasal congestion, wheezing, chest tightness, coughing and throat irritation. Prolonged exposure to high levels of indoor dampness can reduce lung function and cause chronic health problems. Moulds produce allergens, irritants, and sometimes, toxic substances. Inhaling or touching mould spores may cause an allergic reaction, such as sneezing, a runny nose, red eyes and skin rash. Moulds can also cause asthma attacks.

Mould and damp are caused by excess moisture. Moisture in buildings can be caused by leaking pipes, rising damp in basements or ground floors, or rain seeping in because of damage to the roof, or around window frames.

A newly built home may be damp if the water used when building it is still drying out – for example, in the plaster on the walls. Excess moisture indoors can also be caused by condensation.

If you have mould or damp, it is important to find out why you have excess moisture in your home. When you know what's causing the damp, you can make sure your home is repaired or take steps to limit the moisture in the air. You may need to get a professional in to remove mould for you, but if it's only a small amount you may be able to remove it yourself.

EMF[1]

Electromagnetic fields have gained a lot of attention recently, especially with the increase in electrical devices, particularly those with wi-fi in the home. Emfs have different frequencies - higher frequencies have more energy and are considered more harmful than lower frequencies. EMFs cause damage by activating cellular stress responses and also cause breaks in DNA strands. They are associated with chronic inflammation, stress and oxidative stress and are thought to increase the risk of cancers and neuro-degeneration. Research has also associated them with depression, insomnia and headaches.

EMFs are all around us, but some significant sources are Power masts/sub stations/overhead cables, mobile phones, electrical equipment and anything with wi-fi, radio-waves and also microwaves.

HAND SANITISERS

Our skin is home to trillions of microorganisms that compose the skin microbiota. The primary role of the skin is to serve as a physical barrier that helps to protect us from invading pathogens, thus making our skin microbiome an important part of our overall health. Hand sanitisers have become a regular fixture of daily life and an important component of public health. They do, however, contain alcohol, which can damage the natural barrier of the skin. Whilst they play a role in killing potentially harmful pathogens, they do not distinguish between the good and beneficial parts of the skin microbiome, and the bad. It is crucial therefore that we are mindful of the impact they may have on the communities of beneficial bacteria on the skin.

Whilst it is important to follow government guidelines, we recommend using hand sanitizers with caution, and only if other methods of washing your hands are not available. Furthermore, choosing a handwash that does not contain harmful ingredients (triclosan, SLS etc) is also recommended.

DETERGENTS[1-4]

Household products can also be a problem, as they contain ingredients which have been shown to be detrimental to our health.

These can include:

- Phthalates
- Perchloroethylene
- Triclosan (an antibacterial)
- Quaternary ammonium products (products derived from ammonia)
- 2-butoxyethanol
- Chlorine
- Sodium hydroxide

WATER

One of the ways that toxins get into the food chain is through water. The oceans are contaminated with heavy metals, plastics, pesticides, herbicides and sewage, to name a few. When chemicals are put on the land (e.g. pesticides), they eventually run off the land and into rivers and oceans. Freshwater, therefore also contains toxins, including chorine. This can affect all organisms on land and enters the food chain via drinking water, farmed fish, animals and agriculture etc.

EFFECT ON IMMUNITY

Studies have shown:

- Cadmium exposure induces oxidative stress by inhibiting antioxidant activity and down-regulating the expression of key genes involved in the immune response (LYS, C3, TOR, TGF-β, IL-10, TNF-α and IL-8), suggesting inhibited immune defences
- Exposure of ducks to Dichlorodiphenyltrichloroethane (DDT) reduced their resistance to viral infection
- Pesticides CPF and CBZ dose-related reduced macrophage lysosomal enzyme activity and LPS-induced production of IL-1β, TNFα and NO (inflammatory markers)

REDUCE EXPOSURE BY:

- Choosing organic – this can reduce pesticide exposure. Try an organic veg box!
- Filtering drinking water, filters can be installed in taps
- Opt for small cold-water fish e.g. sardines, anchovies and mackerel over farmed or large oceanic fish such as fresh tuna, swordfish and marlin
- Remove exposure to allergens from the diet and environment
- Switch off electrical equipment when not in use
- Reduce toxic household and personal care products. Opt for organic and environmentally friendly brands or it is also possible to make your own
- Ensure foods are fresh and free of mould
- Avoid sleeping in damp rooms

SUPPORT DETOXIFICATION BY THE LIVER

Help improve removal of waste products from the body by:

- Drinking 1.5 - 2 litres of water per day
- Increasing vitamin E foods (avocado, olives, nuts and seeds, leafy greens)
- Increasing vitamin C containing foods (leafy greens, red peppers, citrus fruits)
- Increasing zinc containing foods (fish, legumes, eggs, nuts and seeds)
- Reducing sugar
- Increasing omega-3 fatty acids from oily fish, flax and chia seeds

LIFESTYLE INTERVENTIONS[1]

Toxins stored in fatty tissue can be liberated and removed by increasing blood and lymph circulation. Sweating, can also carry toxins from the tissue to the liver. Some lifestyle interventions can be useful for this including:

- Shower hydrotherapy – where you take a hot shower for 3 minutes then switch to cold for 30 seconds. Repeat cycle 3 times, dry off quickly and go to bed or dress warmly
- Saunas - use low temperature 65-75°C, keep hydrated and stay in for 15 minutes, then come out for a cold-water rinse, repeat for up to an hour
- Dry skin brushing – this stimulates blood and lymph circulation and supports the skin. You can do this by brushing the whole body, once a day with a natural-bristle dry skin brush. Start with the arms, front and back, moving from fingertips to armpit, always brushing towards the heart. Then do each leg, front and back, starting with feet and brushing upward

TIPS FOR KEEPING HEALTHY IN SELF-ISOLATION[1-10]

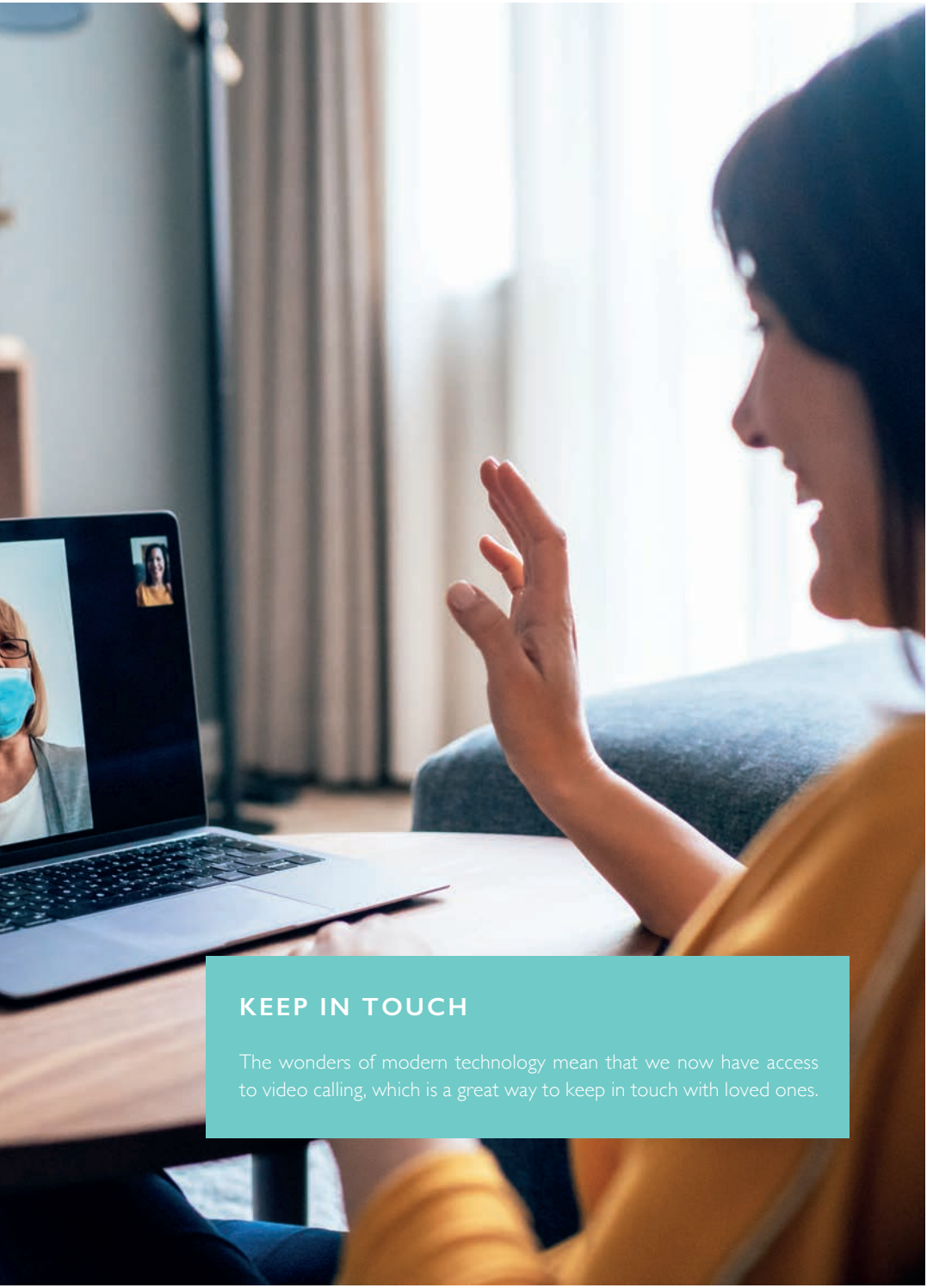
At a time where it is necessary to self-isolate or reduce social contact, it is also essential that we look after our body and also our mind. Although being unable to go about our daily routine, work, to the gym or to socialise seems daunting, depressing and anxiety provoking, it can be an opportunity to step off the daily treadmill and focus on your own wellbeing. This blog aims to provide tools which we can all use to support emotional wellbeing during this difficult time, as well as some to occupy our time.

Keep in touch

It is against human nature to be isolated from others as we have an innate need to be sociable. So, although we may need to be physically isolated, it is important that we still communicate. Feelings of loneliness are greater, and social network size is smaller, among mental health service users than in the general population. Studies have identified an association between loneliness; and depression, suicidal behaviour, personality disorders and psychoses. Among people with severe mental illness, social isolation has been linked to higher levels of delusions, lack of insight and high hospital usage. To put this in simple terms, loneliness significantly affects our mental health. Conversely, people who report greater informal social support have been found more likely to recover from psychotic symptoms. Although you may be physically separated from friends and family, it is important to try and keep in touch.

Write it down

Another lovely thing to do, which has been lost in recent times, is letter writing. If you have an older family member, sending them a letter is a nice way of letting them know you are thinking about them. Writing a letter or drawing a picture for grandparents is also a good activity to get the kids to do. It has also been shown that diary writing is a great way of supporting mental health. In a study looking at 89 participants with previous mental health disorders, individuals who completed a positive writing resource diary had significantly lower depression scores than controls.



KEEP IN TOUCH

The wonders of modern technology mean that we now have access to video calling, which is a great way to keep in touch with loved ones.

Gratitude journals are less intensive than diary writing as they can be done each day in a couple of minutes. Research shows that practising gratitude can help improve measures of stress and depression. It may seem like there is little to be grateful for at the moment, but when you start journaling you will be surprised at how many things there actually are. One study showed that people who were asked to journal five things they were grateful for, that had occurred in the past week, were 25% happier than those who didn't or journaled negative emotions.

It is also useful to keep in touch with your wider community, either in a professional capacity or by finding a subject that you are passionate about. Find a great podcast that catches your interest, helps you improve your knowledge or simply makes you laugh. This keeps your mind active, engaged, entertained and also keeps you in contact with the wider-world.

Meditation/Mindfulness

This is one of the best ways to reduce tension and anxiety and support a healthy mind. However, when we are busy it is one of the things that tends to get pushed to the back of the queue. Mindfulness-based stress reduction can have small positive effects on depression, anxiety and psychological distress.

Mindfulness doesn't have to take much time - you can just do simple breathing exercises. There are many different ways to do this but a simple one is the 4-4-8. This is where you breathe in for the count of four, hold for four and breathe out for eight. Doing this for a minute each day has been shown to reduce symptoms of anxiety.

You can also use an app for directed meditation or mindfulness, if you want to explore this further. There are many apps available, some popular ones are 'Calm' and 'Headspace'. If you are at home with the kids, Calm has a great selection of directed mediation for children.

Gardening

There are many health benefits of gardening including - physical fitness, exposure to nature and sunlight, a sense of doing and achievement and improvements to mental wellbeing. This is something you can also get the children involved in. Spring is a great time for planting seeds and summer bulbs and also for planting some immune-supporting vegetables. Salad leaves and plants, like spring onions, chives and rosemary are great, even if you just have a pot or a window box, and they contain mild antimicrobial properties.

Cooking

Fresh foods are best for your health, so get the family together and start being creative with cooking. This teaches kids great life skills, provides healthy meals and can be much cheaper than processed or take-away foods. If you are struggling to get hold of ingredients and have some tired vegetables in the fridge, boil them up in a stock and you have a soup which you can freeze.

Acts of kindness

These have been strongly shown to improve our mood and wellbeing. Practicing kindness has a profound effect on our mental and physiological health, helping us to become happier and compassionate towards others. Being kind to others has been shown to improve our immune system, slow down ageing, elevate our self-esteem and improve blood pressure. At the moment, the kindest thing we can do is to stay at home and keep away from vulnerable people. However, we can still elicit acts of kindness, such as offering to help with shopping for an elderly neighbour, calling a friend who may be struggling and being kind and patient with other members of our household (offer to make them a cup of tea, for example).

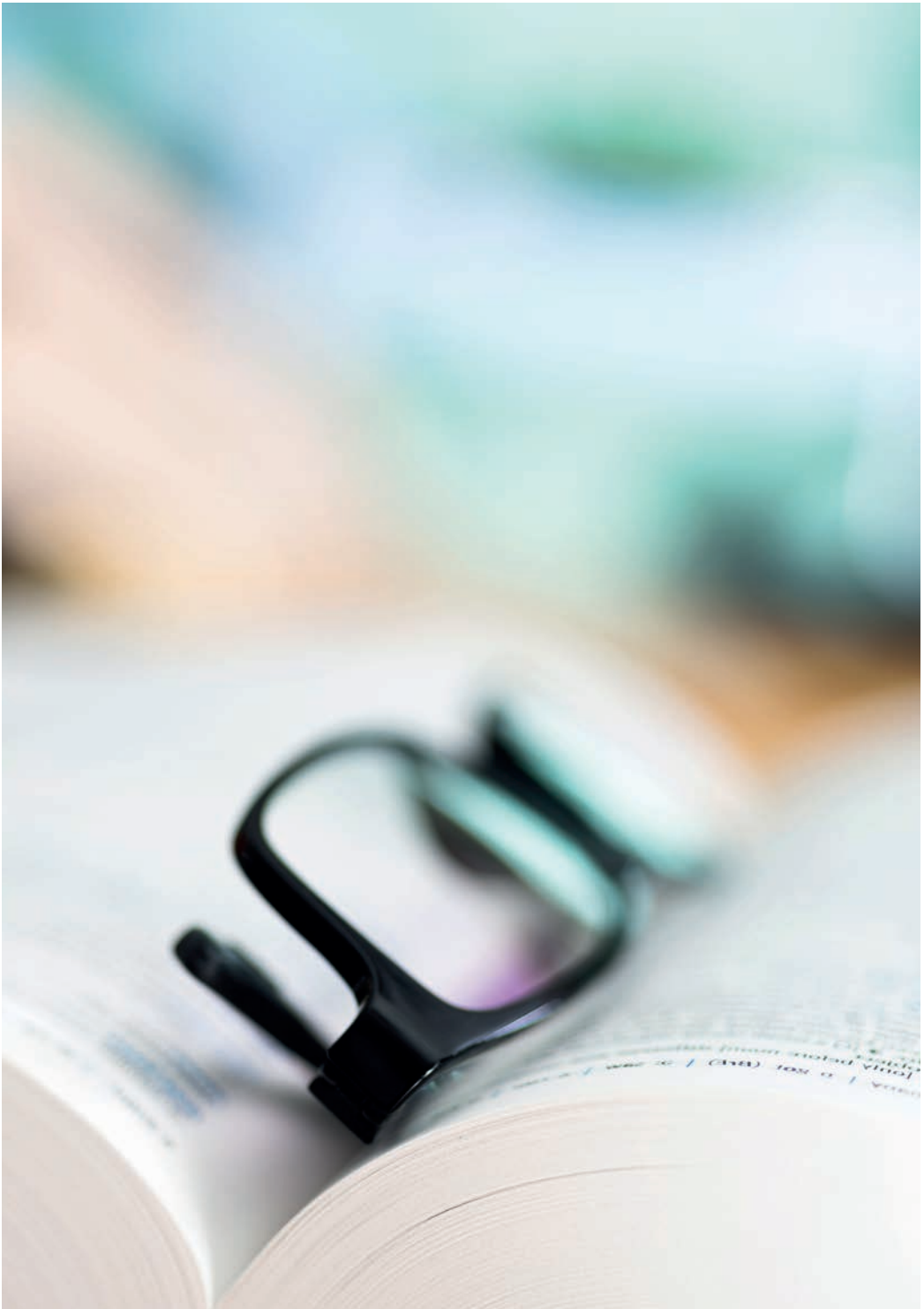
Task setting

Setting small everyday tasks and keeping to a routine can be important for helping us to feel that we have achieved something. It can also help to deter us from a sedentary lifestyle and subsequent low mood. Come up with a list of things that you have been meaning to do for a long time but have been putting off due to lack of time. This may not seem like the most exciting thing to be doing, but it can help you feel like you are being purposeful, which is important for mental wellbeing.

LIST OF ABBREVIATIONS

ACE2	Angiotensin-Converting Enzyme 2
APC	Antigen Presenting Cell
ARDS	Acute Respiratory Distress Syndrome
ARI	Acute Respiratory Tract Infection
B-Cell	B stands for the bursa of Fabricius, which is an organ unique to birds, where B cells mature
CBZ	Carbendazim (fungicide)
CCL	C-C Motif Chemokine Ligand
CD	Cluster of Differentiation
COPD	Chronic Obstructive Pulmonary Disease
CPF	Chlorpyrifos (insecticide)
CR	Complement Receptor
CVD	Cardiovascular Disease
CXCL8	C-X-C Motif Chemokine Ligand 8
DDT	Dichlorodiphenyltrichloroethane
DHA	Docosahexaenoic Acid
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic Acid
FDA	Food and Drug Administration
GABA	Gamma Aminobutyric Acid
GALT	Gut Associated Lymphoid Tissue
GRAS	Generally Recognised as Safe
GMP	Guanosine Monophosphate
H1N1	Hemagglutinin Type 1 Neuraminidase Type 1 (both proteins that are found on the outer shell or envelope of the virus). Often referred to as 'Swine flu'
H1N2	Hemagglutinin Type 1 Neuraminidase Type 2. Often referred to as 'Bird Flu'
HIV	Human Immunodeficiency Virus
HLA-DR	Human Leukocyte Antigen – DR isotype
HPA	Hypothalamic–Pituitary–Adrenal
HSV	Herpes Simplex Virus
ICU	Intensive Care Unit

IFN	Interferon
IL	Interleukin
IV	Intravenous
LPO	Lactoperoxidase
MALT	Mucosal-Associated Lymphoid Tissue
Mpro	Main Protease
MERS	Middle East Respiratory Syndrome
MT	Metallothionein
MNV	Murine Norovirus
NAC	N-Acetylcysteine
NK	Natural Killer cell
NLRP3	Nod-like Receptor Protein 3
NO	Nitric Oxide
PRR	Pattern Recognition Receptors
RAS	Renin-Angiotensin System
RCT	Randomised Controlled Trial
RNA	Ribonucleic acid
SARI	Severe Acute Respiratory Infection
SARS	Severe Acute Respiratory Syndrome
SLS	Sodium Lauryl Sulphate
T-Cell	T stands for thymus - the organ in which these cells mature
TGG	Tetra-O-Galloyl-β-D-Glucose
TH1	T-Helper Cell Type 1
TH2	T-Helper Cell Type 2
TILDA	The Irish Longitudinal Study on Ageing
TNF	Tumour Necrosis Factor
TLR	Toll-Like Receptor
TGF-B	Transforming Growth Factor beta
µg	Microgram
URTI	Upper Respiratory Tract Infection
UVB	Type B ultraviolet
WHO	World Health Organisation
ZIKV	Zika Virus



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NOTES

NOTES

STEP 1. Immunity diet and nutrients

STEP 2. Gut Health and Immunity

STEP 3. Immunity and Sleep

STEP 4. Immunity and Stress

STEP 5. Immunity and Exercise

STEP 6. Keeping your Home Healthy – toxins in the home

PLUS Tips for Keeping Healthy in Self-Isolation