The Functional Medicine Approach to COVID-19: Nutrition and Lifestyle Practices for Strengthening Host Defense

Minich DM[1], Hanaway PJ[2]

[1]*Human Nutrition and Functional Medicine Graduate Program, University of Western States, Portland, OR*
[2]*The Institute for Functional Medicine COVID-19 Task Force, Federal Way, WA*

Abstract

The developing symptoms of COVID-19, as well as the progression of illness and fatality, are a clearly a function of the overall health status of the individual. Complex, chronic diseases such as obesity, hypertension, and diabetes are directly correlated with risk of disease severity and mortality. We explore lifestyle interventions that have specifically been demonstrated to strengthen host defense, reduce the probability and mitigate the severity of viral infection. Lifestyle interventions, from a Functional Medicine perspective, include nutrition, sleep, exercise, stress reduction, and connection. These factors, when in balance, provide a foundation for optimal health and immune function.

Food/Nutrition

Overall Recommendations: Research indicates that plant-based foods such as those high in phytonutrients, water- and lipid-soluble vitamins, and other antioxidants, as well as dietary fiber, can help downregulate an overactive immune response.

Specific recommendations for patients:

1. Eat plenty of fruits and vegetables. Aim for 9-13 servings per day of a variety of types for a wide array of phytonutrients to enhance the gut microbiome.
2. Consume dietary fiber, a minimum of 28-35 grams daily, preferably from whole foods.
3. Eat fermented vegetables or other probiotic-containing foods to maintain epithelial health and gut barrier function.
4. Reduce or avoid immune offenders such as added sugars and salt, high-glycemic foods (including processed carbohydrates), and excessive saturated fat.

Food and nutrition are major daily input for health and well-being. There are three mechanisms that may be involved in the ability of food-derived compounds to reduce viral infection and severity:

1. Balancing inflammatory pathways.
2. Reducing oxidative stress and increasing antioxidant levels.
3. Harmonizing the gut microbiome.

Balancing Inflammatory Pathways

Inflammation and immune responses often occur together in a viral infection. While inflammation is required in the initial stages of an immune reaction to infection, prolonged release of inflammatory mediators (e.g., interleukins, prostaglandins, tumor necrosis factor-alpha [TNF-alpha]) may cause system-wide perturbations. Low-level chronic inflammation and activation of the innate immune response are suggested mechanisms for increased risk of lifestyle-induced diseases such as type 2 diabetes.[1] Therefore, to lower inflammatory load, clinicians suggest refraining from eating a Westernized diet[2] and shifting toward a balanced dietary pattern resembling the well-studied Mediterranean diet.[3,4,5]

Furthermore, data from the Nurses' Health Study suggests that an inflammatory dietary pattern has been identified as one that is high in "sugar-sweetened soft drinks, refined grains, diet soft drinks, and processed meat but low in wine, coffee, cruciferous vegetables, and yellow vegetables."[1] Therefore, reducing or omitting foods that negatively impact the inflammatory cascade—such as those containing added sugars,[6] salt,[4] or trans fats,[7] as well as those that have a high glycemic index[8] or excessive amounts of saturated fats[8]—would be helpful in lessening the overall inflammatory burden. A systematic review has shown that a single, high-fat processed meal (e.g., a meal consisting of white bread, butter, cheese, and a milkshake) leads to increases in the inflammatory cytokine interleukin-6 (IL-6) of around 100% relative to baseline within six hours of eating.9 Given that many pesticides are also known to impact immune function, increasing consumption of organically grown produce may lower the inflammatory burden and improve immune function.[10]

As part of maintaining the balance of inflammation, the omega-6 to omega-3 fatty acid ratio needs to be evaluated. A low ratio of omega-6 relative to omega-3 fats can shift the production of prostaglandins from the series-2 (inflammatory) to the series-3 (anti-inflammatory) compounds.[11] Simopoulos[11] recommends an omega-6:omega-3 ratio of 1:1 to 2:1, which is in alignment with traditional diets. Another dietary factor shown to be inflammatory, particularly in those with autoimmune disease, is salt (sodium chloride) intake,[4] due to its ability to induce pathogenic T helper 17 (Th17) cells.[12]

In conjunction with avoiding foods that provoke inflammation, increasing foods with known anti-inflammatory effects may be beneficial. These include plant-based foods such as fruits, vegetables, and legumes,[13] which contain phytonutrients shown to have anti-inflammatory effects such as polyphenols[14] and flavonoids.[15] In a study of healthy European adolescents, the pro/anti-inflammatory ratio was inversely associated with dietary intake of polyphenols.[16] Even adding plant-based, anti-inflammatory foods to an inflammatory meal may offset the impact. For example, high intakes of fat and carbohydrates have been shown to stimulate markers of innate immunity, particularly the toll-like receptor (TLR) families.[4] However, adding in orange juice to a high-fat, high-carbohydrate meal was shown to blunt the typical release of endotoxin, potentially due to the flavonoid content of the juice.[17]

Reducing Oxidative Stress And Increasing Antioxidant Levels

One of the initial aspects in viral infection is what is referred to as a "cytokine storm," or an abundance of oxidative stress, which can produce damaging free radical compounds such as reactive oxygen and nitrogen species (ROS/RNS). To alleviate oxidative stress, it is important to consider a two-pronged approach:

- Reducing food-derived oxidative compounds.
- Fortifying the body's reserves of antioxidants.

First, it's important to adjust food preparation measures. Grilling, frying, and broiling, as opposed to boiling and steaming, can create oxidative compounds referred to as advanced glycation end products (AGEs). These resulting dietary oxidative compounds can provoke an inflammatory response of human innate immune cells.[18] Therefore, cooking foods at lower temperatures and using moist methods of food preparation rather than dry, hot heat may be helpful for reducing their production. In a crossover intervention trial with 62 healthy subjects, a steamed diet versus a diet containing the same foods treated with high heat showed the latter caused lower insulin sensitivity, omega-3 levels, and levels of vitamins C and E.[19]

Secondly, including antioxidant-rich, nutrient-dense foods in the daily diet, such as those from plants, may be a helpful measure for crowding out nutrient-depleted foods and reducing oxidative injury.[20,21] Antioxidants can be vitamins or phytonutrients that are water-soluble (e.g., vitamin C) or fat-soluble (e.g., carotenoids, tocopherols, tocotrienols) in nature. An analysis of 1 113 food samples[21] revealed the following food categories as some of the highest in antioxidants (listed in order of level):

- Spices/herbs
- Nuts/seeds
- Chocolate
- Vegetables

Conversely, the food categories with the lowest antioxidants were fats/oils, meats, poultry, fish/seafood, and eggs.[21] Of the specific foods highest in antioxidant content (containing >10 mmol antioxidants/100 g), most were spices: ground cloves, dried oregano, ground ginger, ground cinnamon, turmeric powder, walnuts, dried basil, and ground mustard seed.[21] Red wine and brewed coffee were among the top 50 as well.[21]

Harmonizing the gut microbiome

Since the gastrointestinal tract harbors a majority of immune system activity, it is essential to keep it nourished with the necessary nutrients for a healthy gut microbiome.[4] Dietary fibers from whole, plant-based foods can be fermented by bacteria for energy, resulting in the production of short-chain fatty acids (SCFAs) that have pleiotropic effects, including positively influencing epithelial barrier function and reducing pathogen cytotoxicity from compounds produced by harmful bacteria.[22] Butyrate is one of these SCFAs with immune-modulating activities, including improving gut barrier function and innate immunity.[23] High-fiber diets can directly modulate immune reactivity by increasing levels of SCFAs, which can activate the G protein–coupled receptors on various tissues, including immune cells.[22] Further, SCFAs have epigenetic effects, which could ultimately alter immune cell function.[22] Recommendations for fiber intake are for a minimum of 14 grams per 1,000 kcal, or approximately 25-35 grams daily for most individuals.[24]

Fermented foods such as yogurt, kefir, kimchi, miso, and sauerkraut may provide microorganisms and secondary metabolites such as alkyl catechols[25] that may help with immune response and even reduce the incidence and duration of respiratory infections.[26] Lactic acid, which is a byproduct of fermentation, has been shown to reduce pathogen growth in the oral cavity, oropharynx, and esophagus.[27] Furthermore, specific strains of microorganisms may impact specific viruses[28] and may be important for targeted actions related to immune function. For example, a kefir containing six lactic acid bacteria strains resulted in increased natural killer cell activity and interferon-gamma secretion in response to tumor cells.[29] In general, probiotic microorganisms within the *Lactobacillus* and *Bifidobacterium* species have been demonstrated to exhibit numerous beneficial effects on immunity through their interactions with macrophages, enterocytes, and dendritic cells, as well as Th1, Th2, and regulatory T (Treg) cells.[30]

A Note About Plant-Derived Compounds And Immunity

Polyphenols

As discussed above, a common thread throughout the mechanisms related to immunity relates to the anti-inflammatory, antioxidant, and gut-balancing effects of plant-based foods. Specifically, plant foods contain thousands of phytonutrients, which have been categorized into phytonutrient families. One of the groups of plant compounds shown to be helpful for immunity is polyphenols, a category consisting of more than 8,000 different compounds such as flavonoids (e.g., isoflavones and anthocyanins) and non-flavonoids (e.g., phenolic acids and stilbenes).[31] These phenolic compounds are ubiquitously found in plant foods like fruits, vegetables, nuts, seeds, legumes, and whole grains. On a physiological level, they can serve as foodstuff for the gut microbiome, resulting in the metabolic production of favorable metabolites for immune enhancement. At the molecular level, they are thought to regulate immune function through several mechanisms, including favorably modifying proinflammatory pathways involving nuclear factor-kappa beta (NF-kB), mitogen-activated protein kinase (MAPK), and arachidonic acid, along with suppressing TLR.[31] Coupled with their anti-inflammatory properties, they can inhibit oxidative enzymes responsible for free radical generation, such as xanthine oxidase and NADPH oxidase, while stimulating the endogenous production of helpful antioxidant enzymes like superoxide dismutase.[31] Examples of food-based polyphenols with immune-regulating activity include quercetin (e.g., apples and onions), resveratrol (e.g., grapes), epigallocatechin-3-gallate (green tea), and curcumin (turmeric).[31]

Plant Dietary Diversity

What is key for immunity is not just ensuring the intake of plant-based foods in the diet but getting a diverse blend of plant compounds for the gut microbiome. As stated by Heiman and Greenway,[32] "*The more diverse the diet, the more diverse the microbiome and the more adaptable it will be to perturbations*." The gut microflora can be modified through dietary components and, ultimately, significantly impact markers of metabolic health that relate to inflammation.[33] For example, in one clinical trial with Danish adults, it was found that those who had a less diverse gut microbiome also had an inflammatory phenotype and greater metabolic dysfunction, including adiposity and ability to gain weight, insulin resistance, and dyslipidemia.[33] Another clinical trial in overweight and obese individuals indicated that less microbial gene diversity (40% lower) was associated with increased metabolic dysfunction and inflammation.[34] The researchers suggested that dietary intervention may be helpful for improving microbial gene richness.[34]

Unfortunately, our exposure to plant varieties has significantly decreased over time from several thousand to mere hundreds, with most of the food in the world coming from fewer than twenty plant and animal species combined.[32] As is typically advised with food intolerance and/or allergy, rotating plant foods in the diet every three to four days may be important in ultimately conferring greater immune resilience. Having greater dietary diversity may also ensure better nutrient status[35,36] and lower rates of allergic disease, as has been demonstrated in children.[37,38]

Moreover, some may contend that meeting daily servings of fruits and vegetables is sufficient; however, a study[39] in healthy women suggests that diversity is a major factor. The women were divided into two arms, each consuming 8-10 servings of fruits and vegetables but with different levels of botanical diversity, with one group having five botanical families and the other group having selections from eighteen botanical families. While both diets were helpful in reducing lipid peroxidation, the higher diversity diet resulted in a significant decrease in DNA oxidation specifically.[39] As a general guideline, it has been suggested to encourage patients to aim for 50 unique, plant-based foods in a week.[40]

Download Patient Education Tools: Lifestyle Practices for Strengthening Host Defense[i]

Stress Reduction/Management

Overall Recommendations: Both acute and chronic stress can result in dysregulated, suppressed immune function. Under these conditions, susceptibility to illness is more likely. Monitoring stress levels through biofeedback markers such as heart rate variability (HRV) may assist in knowing when to implement stress management strategies and in having a means to assess their efficacy, as well in helping to track resilience-building approaches. Practicing stress-modifying techniques on a regular basis using HRV and other modalities can result in greater resilience when confronted with stressors.

In 1936, Hans Selye defined stress as the nonspecific response to change. Some degree of stress may be healthy for normal functioning and even beneficial for immunity (referred to as 'hormesis'),[41] while chronic, low-level stress without resolution or coping behaviors may suppress immune function.[42] Hence, the field of

i. https://info.ifm.org/covid-19#patientEducation psychoneuroimmunology was created decades ago to acknowledge the effects of psychological distress on health conditions, primarily through the mechanism of increased inflammation.[43]

It is now well established that these stress states can significantly alter not just wound healing but exacerbate inflammatory immune states such as autoimmune disease, asthma, and allergy.[44] They have also been implicated in the morbidity and mortality seen in diseases of immune dysregulation, including cancer, HIV, and inflammatory bowel disease.[45] More specifically, chronic stress is associated with increased risk of viral infection like the common cold.[46] Furthermore, stress affects both respiratory disease susceptibility and severity.[47]

There are several proposed mechanisms by which stress impacts immune function. In general, earlier scientific discussion alluded to stress as immunosuppressive.[45] More recent thinking suggests that stress causes immune dysregulation or an 'inappropriate' response, such as shifting the Th1/Th2 cytokine balance toward the Th2 side, resulting in lowered defense against infection and increasing hypersensitivity diseases.[45] For example, even a brief mental stress condition in healthy adults can significantly reduce Treg cells, resulting in less self-tolerance and greater propensity toward autoimmune conditions.[48]

The process of stress is two-fold. First, the sympathetic nervous system stimulates the release of epinephrine and norepinephrine. These compounds activate inflammation through the production of transcription factors that bind to genes to increase the synthesis of inflammatory cytokines. Second, the hypothalamus-pituitary-adrenal (HPA) axis produces glucocorticoids like cortisol. Long-term secretion of these compounds can lead to lower proinflammatory cytokines (which are needed at the start of infection), matrix metalloproteinase activity, bacterial peptide activation, hypoxia,[49] and, eventually, higher risk for infection, inflammatory-based diseases, accelerated aging, and even early mortality.[50]

Due to the chronically elevated baseline of stress that most people have and fail to recognize because they have become accustomed to higher levels over time (allostasis), it is helpful to have assessments that gauge stress level. Simple pen-and-paper tests are available through the IFM Toolkit or through the American Institute of Stress.[51] There are also biofeedback and metric devices such as heart rate variability (HRV) technologies and even continuous HRV monitors to provide an indication of the overall balance of the autonomic nervous system. HRV is a known marker for a variety of health outcomes, including loss of vagal activation and heightened release of inflammatory markers.[52] In a study with 30 healthy women subjected to an acute psychosocial stressor, reductions in HRV measurements during the stressor were associated with elevated levels of TNF-alpha and IL-6 just one hour after being exposed to the stressor.[53] Therefore, HRV may provide an opportunity to monitor one's resilience, or one's ability to effectively respond to a stressor through production of inflammatory markers.

Whereas an inability to regulate emotional states and labile mood have been associated with immune system suppression and virus shedding,[54,55] stress reduction and/or management has been shown to reduce infection and the severity of infection. A systematic review of mind-body practices indicated that several practices such as yoga, meditation, mindfulness, tai chi, qigong, relaxation response, and breath regulation result in favorable gene expression patterns that benefit immune regulation.[50] At the molecular level, these practices downregulate NF-kB and positively influence a set of molecular factors referred to as a conserved transcriptional response to adversity (CTRA), known to be associated with less resistance to viral infections from herpes simplex viruses, HIV-1, Epstein-Barr virus, and cytomegalovirus, to name a few.[50] In a small study with long-term qigong practitioners versus controls who did not practice, it was shown that the qigong practitioners had 132 downregulated and 118 upregulated genes (of the 12 000 genes measured in neutrophils, which are most important in fighting infection) that translated into improved immune response and even delayed cell death.[56] Several studies have found that gardening may contribute to a sense of mental and physical well-being,[57-60] as well as improving mood and reducing stress.[61] Overall, the collective literature on these mind-body and stress reducing practices would suggest that favorable responses come with repetition and consistent practice.[50]

Sleep

Overall Recommendations: Due to its restorative and regulatory abilities, sleep has a major influence on immune function and inflammatory signals. Therefore, getting good quality, sufficient quantity (seven to eight hours) and adequate deep phasic bouts of sleep is of utmost importance as part of immune maintenance, as well as during times of recovery from illness. It is advised to have patients practice good sleep hygiene and maintain consistent sleep hours by turning off screens, ensuring the room is cool, quiet, and dark, and setting reminders to go to bed on time.

One of the common recommendations from experts when it comes to improving immune function is to ensure good quality (e.g., perceived quality as much as adequate deep rapid eye movement [REM] sleep) and sufficient quantity of sleep due to the bidirectional relationship between sleep and immunity.[62,63] Sleep is inherently restorative and enables an internal resetting or regulatory aspect of one's physiology. There is substantial evidence to suggest that sleep disturbance such as insomnia or lack of quality sleep, or even one night of reduced sleep, is associated with disturbances in the innate immune system due to disruptions in the circadian homeostasis of inflammatory cytokines and in the activities of immune cell subpopulations (e.g., CD4+, CD8+, and natural killer [NK] cells).[62,64] Viral infections may present with symptoms such as fever and pain that may interfere with sleep patterns.[63] Medications such as corticosteroids and analgesics may also negatively impact one's ability to sleep. In those with hepatitis C virus–related neurological dysfunction, about half exhibit abnormal sleep rhythms.[65] Moreover, the virus itself may cause physiological shifts in sleep. For example, earlier research with animals showed that intranasal exposure to the influenza virus led to subsequent changes in the proportion of non-REM sleep and REM sleep.[66] In a small human clinical trial with individuals injected intranasally with a particular rhinovirus, those who developed symptoms had sleep time reductions of 23 minutes, consolidated sleep decreases of 36 minutes, and overall sleep efficiency reduced by 5%.[67]

Furthermore, there can be complex interactions between sleep disturbance and other lifestyle factors, such as social connectivity. For example, Irwin and Opp[64] demonstrated an association between improved sleep efficiency and lower IL-6 production, which was particularly enhanced in those with positive social relationships. Conversely, women who had poor social relationships had greater sleep inefficiency and even higher IL-6 levels. Interestingly, there was a compensatory effect for healthy social networks, even in the groups with poor sleep. In other words, even when sleep efficiency was poor, the levels of IL-6 could be modulated through having good relationships. Similarly, those who had good sleep but poor social relations had lower IL-6.[64]

Collectively, while the findings have been mixed, a host of studies have indicated greater inflammatory cytokines occurring with shorter sleep duration (defined as less than five to six hours per night) compared with seven to eight hours.[63,68,69] Moreover, it is worthwhile to note that *perception* of the quality of one's sleep is important, as upregulated white blood cell counts have been shown to be associated with subjective accounts of sleep quality.[70] Even after a bout of sleep restriction, it may take more than a night or even three nights of sleeping longer (such as eight to ten hours) to resolve any neurobehavioral issues related to the sleep deficiency.[71-73] In some cases, immune cell activity of certain types can be restored short-term after sleep depletion.[74,75]

Exercise

Overall Recommendations: Moderate, regular physical activity helps immune system function by raising levels of infection-fighting white blood cells and antibodies, increasing circulation, and decreasing stress hormones. A personalized exercise program can be designed even during homestay by utilizing features in one's home environment, including apps, the internet, and technology, or by taking the opportunity to experience the calming, immune-supportive effects of being in nature (while, at the same time, social distancing).

Physical activity provides the movement the body needs to oxygenate, circulate blood and nutrients, and eliminate waste from cells, all of which are essential to the function of the immune system. In addition to the blood vessels delivering blood to organ systems, the lymphatic system, present largely in the neck, armpits, and groin, plays a big role in the transport of immune factors. Indeed, the social distancing and homestay that has been recommended by many states and nations may invariably disrupt people's activity schedules and lead to more sedentary behavior, such as more screen time or sitting, reclining, or being stationary, which could further negatively impact immune activity.[76]

According to a recent interview[77] with Jeffrey Woods, PhD, a professor who researches the effects of exercise on immune response at the University of Illinois at Urbana-Champaign, it is important and safe to be exercising during the coronavirus pandemic, especially for those who are regular exercisers. For those who are sedentary, he comments, "*If you are sedentary, it may be a good idea not to overdo it. Research suggests that unaccustomed strenuous or prolonged exercise might reduce the function of your immune system defenses*." For those who are infected with COVID-19 and have upper respiratory tract symptoms that are mild (e.g., sinus congestion, runny nose), he recommends moderate exercise, but not for those with severe symptoms (e.g., body aches, fever, chest cough, fatigue, or shortness of breath).

Research has shown that a single bout of physical activity can stimulate immune function due to the rapid cellular changes that take place,[78] but regular exercise is much more robust in its effects on immunity.[79,80] There continues to be debate about the intensity of activity and whether high-intensity activity in untrained individuals is indicated. For highly fit individuals, continuation of intensity may not be problematic; however, for those who are more sedentary or ill, it remains unknown as to whether the initiation of an exercise program at greater intensity of activity would be helpful or if it would be physiologically stressful.[77,81] While the effects of initiating high-intensity physical activity in a sedentary person remain unknown, it would seem prudent to start some kind of exercise program regardless because of the plethora of findings that support the benefit of physical activity for the immune system. Even in healthy individuals, too much strenuous exercise has been associated with immunosuppression when compared to controls leading their normal lifestyle.[82] In the absence of rigorous data, it is most likely best to tailor activity duration and intensity to the individual.

The preponderance of data is on the effect of aerobic activity on immune health.[77,83] At this time, there are preliminary reports of tai chi/qigong and yoga assisting with immune function. In a study with 50 older adults assigned to either a control or tai chi/qigong group for five months,[84] the group assigned the activity had improved antibody response to an influenza vaccine that was administered within the first week of intervention. Furthermore, a systematic review of 15 studies on yoga found that it can lead to a pattern of inflammation downregulation, including lower IL-1beta, TNF-alpha, and IL-6, as well as enhancements in immunity.[85] The authors concluded, "*These results imply that yoga may be implemented as a complementary intervention for populations at risk or already suffering from diseases with an inflammatory component*."

Due to the constraints brought on by the COVID-19 pandemic, exercise may need to be adjusted to fit a home-based schedule.[86] Suggestions include stretching, walking in nature, stair climbing, chair squats, and even simple yoga poses since they require no equipment. There are many online offerings through apps and the internet to engage in classes if more interaction is desired.[87] Furthermore, this time of social distancing may be optimal for being in nature to experience the therapeutic effects (referred to as Shinrin-yoku, or forest bathing), such as an increase in NK cell activity, physiological relaxation, immune recovery, and a decrease in stress.[88] Dr. Steven Blair's quote from Dr. Ken Powell,[89] "*Some activity is better than none, and more is better than less,*" seems to be particularly relevant during these times of quarantine and the resulting risk of increased sedentary behavior. Ideally, 30 minutes of physical activity every day, or a total of 150 minutes weekly, should serve as a guideline for most individuals.[90]

Social Factors/ Connection

Overall Recommendations: Social connections are important to consider and evaluate with patients as part of their health status. In some cases, interactions with others will be supportive, and in other instances, there may be conflict or stress. For immune health, the focus should be on reducing exposure to interactions perceived as hostile and non-supportive and, at the same time, on emphasizing and encouraging time with others who are positive or affirming. For those people who may be lonely or isolated, such as the elderly, as well as those who may be at increased risk of immune compromise, providing ideas for regular social connection may be helpful for establishing a routine. Ideas might include participating virtually in local community events or in a religious or spiritual group.

Social relationships are a significant determinant of immune health. The absence of these essential relationships, collectively referred to as social isolation, loneliness, bereavement, and/or conflict, has been implicated in the upregulation of proinflammatory processes[91,92] and reduced immune functionality (e.g., NK cell activity).[93] Furthermore, those who are socially isolated have heightened response to stressors.[92] Older individuals may be particularly at risk for the effects of loneliness if their immune system is already compromised.[94,95]

Excessive social interaction may confer either immune benefit or harm through increased exposure to potential pathogens depending on whether or not conflict or stressors are present.[91,93] There is the viewpoint that an individual who is socially interacting with others may, in fact, have the potential for greater antiviral immunity, although much is determined by the individual's environmental exposures, toxic burden, and even genotype. Interestingly, during bouts of increased inflammation, as during illness, there is some instinctual inclination within most people to socially withdraw. The amygdala region of the brain is part of this sickness-induced social withdrawal process and may even be protective by encouraging retreat from threatening images.[96] Therefore, it may be important to personalize exposure to social influences depending on the circumstances, including the current state of health or illness.

The converse of social isolation is to have support and connection, which can come through a variety of means, such as family and friends, community, and spiritual or religious practices. Overall, research indicates that individuals who feel this sense of interconnection, either horizontally with other people or vertically through a sense of something greater than themselves, have favorable gene expression, decreased stress, increased antibodies, and better health outcomes.[97] In a study of over 8 000 adults, greater social engagement and cohabitation were associated with lower C-reactive protein, fibrinogen, and white blood cells.[98] In a study of 155 adults, a positive relationship was found between sociability and salivary secretory immunoglobulin A, an essential feature of mucosal immunity.[99]

The sum of the research on connection and the immune-inflammatory response is mixed as this connection appears to be influenced by several factors, including the response of the individual and their preferences, personality, and health state, as well as whether or not there is conflict or stress in the interactions. However, if there is a sense of supportive connection through the social network, it appears that immune markers can be favorably influenced.

Summary

In general, lifestyle interventions can be an effective means to help patients regain their locus of control during times of uncertainty like those experienced in a pandemic. Substantial research indicates that certain dietary patterns and lifestyle patterns offer viable options for improving overall health, especially by reducing inflammation. The anti-inflammatory effects of foods and aspects of how one chooses to live may, in turn, favorably influence and support immune system function as a preventative measure for reducing the risk of illness. Furthermore, in the case of (viral) infection, implementing these changes could significantly offset the severity and sequelae incurred from illness.

While this unprecedented COVID-19 pandemic may be stressful and have mental-emotional ramifications both short- and long-term for individuals, practitioners can effectively use this time as an opportunity to redirect patients' efforts into an evaluation of their current lifestyle and motivate to make changes that will reduce the immediate risk from acute viral infection, as well as the long term risk of chronic disease.

Summary of Clinician Recommendations

Nutrition

- Eat plenty of fruits and vegetables. Aim for 9-13 servings per day of a variety of types for a wide array of phytonutrients to enhance the gut microbiome.
- Consume dietary fiber, a minimum of 28-35 grams daily, preferably from whole foods.
- Eat fermented vegetables or other probiotic-containing foods to maintain epithelial health and gut barrier function.
- Reduce or avoid immune offenders such as added sugars and salt, high-glycemic foods (including processed carbohydrates), and excessive saturated fat.

Stress Reduction/Management

- Monitoring stress levels through biofeedback markers such as heart rate variability (HRV) may assist in knowing when to implement stress management strategies and in having a means to assess their efficacy, as well in helping to track resilience-building approaches.
- Practicing stress-modifying techniques on a regular basis using HRV and other modalities can result in greater resilience when confronted with stressors.

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- Good quality, sufficient quantity (seven to eight hours) and adequate deep phasic bouts of sleep is of utmost importance as part of immune maintenance, as well as during times of recovery from illness.
- It is advised to have patients practice good sleep hygiene and maintain consistent sleep hours by turning off screens, ensuring the room is cool, quiet, and dark, and setting reminders to go to bed on time.

Exercise

- A personalized exercise program can be designed even during homestay by utilizing features in one's home environment, including apps, the internet, and technology, or by taking the opportunity to experience the calming, immune-supportive effects of being in nature (while, at the same time, social distancing).

Social Factors/Connection

- Reduce exposure to interactions perceived as hostile and non-supportive and, at the same time, on emphasizing and encouraging time with others who are positive or affirming.
- For those people who may be lonely or isolated, as well as those who may be at increased risk of immune compromise, recommend regular social connection as a routine.
- Ideas might include participating virtually in local community events or in a religious or spiritual group.

This resource is only intended to identify lifestyle practices that may boost your immune system. It is not meant to recommend any treatments, nor have any of these been proven effective against COVID-19. None of these practices are intended to be used in lieu of other recommended treatments. Always consult your physician or healthcare provider prior to initiation. For up-to-date information on COVID-19, please consult the Centers for Disease Control and Prevention at http://www.cdc.gov/.

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