Integrative Health and Your Immune System

Overview

An Integrative Health approach to the immune system emphasizes clean living, healthy eating, adequate sleep, exercise, positive relationships, and stress reduction. It draws in mindful awareness and self-care along with conventional and integrative approaches to health and well-being. The Circle of Health highlights eight areas of self-care: Surroundings; Personal Development; Nutrition; Recharge; Family Friends, & Co-Workers; Spirit & Soul; Mind & Emotions; and Physical Activity. This overview explores what a how to apply the latest research on complementary and integrative health (CIH) to immune system health.

Note that this overview focuses immune system health in general. In addition, there are specific Integrative Health tools focusing on some of the more common immune system-related concerns that lead people to see clinicians. For more details on sinusitis, herpes simplex virus, asthma, allergies, upper respiratory infection prevention, urinary tract infections, and herbs that support the immune system, see the specific Immune Health tools that accompany this overview.

Meet the Patient

Joanne is a 45-year-old executive assistant who is new to your practice. She is feeling frustrated with her propensity toward frequent upper respiratory tract infections (URI) and difficulty controlling her asthma. For the last couple of months, she has found herself using her albuterol inhaler 3-4 times per week, maybe a bit more when she was having URI symptoms—which was about three discrete episodes over that time frame. She has had periods similar to that nearly every year for the last 10 years. She denies ever being hospitalized for his asthma, although there were several times over the last 20 years when she required prednisone for an acute exacerbation. She has tried some over-the-counter antihistamines, which seem to help a bit, but she does not like the way they make her feel. She has been on an inhaled steroid in the past but stopped a couple years ago because she was feeling better.

Joanne notes she feels overall fatigued, and she is tired of “always having a cold” and “getting whatever everyone else has, only worse.” She wonders if something is wrong with her immune system that is causing this. She would like to have the energy to play with her children and not be afraid that exercise will worsen her breathing. Clinicians have put her on inhaled steroids when she has had previous episodes, which provided some relief, but she feels this was a really passive approach and may not be getting at an underlying health issue.

Personal Health Inventory

On her Personal Health Inventory (PHI), Joanne rates herself a 2 out of 5 for her overall physical well-being and a 3 for overall mental and emotional well-being. When asked what matters most to her and why she wants to be healthy, she responds:

> *"Feeling like a strong, healthy person that my kids can see as an example of good health and strength. My family, my wife, and children are important to me. My relationships with my brother and my dad are important too, but those have been trickier lately."*

For the eight areas of self-care, Joanne rates herself on where she is, and where she would like to be. She decides to first focus on the areas of Physical Activity and Mind and Emotions by training for a bike race. She also plans to work with her doctor to better understand her asthma and find ways reduce her symptoms.

For more information, review Joanne's PHI.

Introduction

The human immune system is an elegant and complicated defense that not only protects us from foreign invaders such as bacteria, viruses, and parasites, but also is largely responsible for repair of the daily wear and tear from typical use of the body and healing of injuries. The immune system also continually patrols the body to find, and essentially destroy, cells that show signs of having lost regulatory mechanisms that, eventually, may be the seeds of cancer.

The anatomy of the immune system includes a variety of components including, but not limited to, the following:

Specific cell types that circulate in the blood and patrol local tissues: Generally termed leukocytes (aka, white blood cells), these cells types can be generally broken down into components of innate and adaptive immune responses.

a. The **innate immune response** is nonspecific and includes cells that can quickly recognize threats such as cancerous cells and invading infections. They recognize general patterns that pose threats and respond generically by isolating and/or destroying their target. Cell types involved in this response include neutrophils, eosinophils, mast cells, natural killer cells and macrophages. Through activation and inflammation, they produce effector molecules such as prostaglandins and leukotrienes—some of which are inflammatory and some of which control inflammation.

b. The **adaptive immune response** is more specific, generally triggered by the innate immune response (if it becomes overwhelmed) and takes longer to be activated (in the realm of days). It also holds "memory" so that if encountering the same threat in the future, it activates much more quickly. This aspect of the immune system is what we refer to when we are "immune" to a disease through vaccination or previous exposure to an illness (e.g., chicken pox). The main cell types are B cells and T cell (aka lymphocytes).

c. The **innate and adaptive systems** work together and communicate through soluble molecules called cytokines. They also give feedback on each other to regulate the responses to avoid over-reaction or persistence of inflammation.[1]

Physical Barriers: Separations between the external work and our internal environments. This includes our skin and the linings of our respiratory and gastrointestinal (GI) tracts. These barriers are more than a simple layer of cells—they include secreted coatings, molecules, and a complex balance of bacteria called a microbiome that influence local and systemic immune function.

Solid organs and areas of concentrated immune activity:

a. **Lymph nodes**: These small nodules, found all over the body, serve as a place for T and B cells to meet antigens. Also within these nodes, lymphocytes increase in number as needed in response to infections, and usually are clustered in groups at sites where numerous blood and lymph vessels converge such as in the neck axilla and groin among other areas.

b. **Thymus**: This organ found within the chest cavity grows until puberty, then progressively involutes until adulthood when it is largely fatty tissue and a small amount of remaining immune tissue. The main role of the thymus is to select out T cells that are able to recognize self vs, non-self—i.e., assure we have an army of T cells that can recognize invaders and avoid attacking us.

c. **Spleen**: About the size of a fist, the spleen is located in the left upper quadrant of the abdomen. It functions similarly to lymph nodes as a meeting place for antigens, T cells and B cells and a place for lymphocyte proliferation, but it does not connect to the lymph system. While it contains about 25% of total lymphocytes, it also contains high numbers of macrophages. This combination of functions makes the spleen a sort of infection filter for the blood.

d. **Mucosa-associated lymphoid tissue** (MALT): These specialized components of the immune system that line the respiratory, gastrointestinal (GALT), and reproductive tracts.[1]

When the system is underactive, we are obviously more vulnerable to immune system diseases. However, “too much of a good thing” can have adverse consequences as well.

Acute inflammation, as in the case of the swelling that comes after a twisted ankle or the activation of the immune system in an episode of strep throat, is part of the healing process. A low level of chronic inflammation, however, without useful purpose to the individual, is something different. The literature defines this type as two- to fourfold elevation in circulating levels of proinflammatory and anti-inflammatory cytokines, natural occurring cytokine antagonists, and acute-phase proteins, as well as minor increases in counts of neutrophils and natural killer cells. The level of these increases are far from those seen in acute infections or injuries but are strongly associated with various lifestyle and demographic factors and with increased risk of heart disease, diabetes, and chronic obstructive pulmonary disease (COPD),

and all-cause mortality.[2] Immune function, therefore, is crucial to maintain and optimize. Here we will take a deeper look into ways in which various aspects of our lives can support or inhibit optimal immune function.

Chronic inflammation makes a significant contribution to the progress of many common chronic diseases, including cardiovascular disease, stroke, diabetes, depression, cancer, and various types of arthritis.

Self-Care

Physical Activity

The impact of exercise on immune function has several areas to consider. We will start with the example of the risk of acquiring an acute illness such as an upper respiratory infection (URI) or the common cold. Growing evidence indicates that moderate amounts of regular exercise improve immune function and decrease the risk of developing a URI.[3] There is a transient depression of immune function with associated *increased* risk of URI after periods of intense, prolonged exercise such as training for and/or running in a marathon.[4] It appears that exercise lasting more than an hour mildly suppresses lymphocyte proliferation.[5] However, more-recent evidence suggests improved immunity in intensely training athletes, even in those training with the added hypoxic stress of being at altitude.[6] Of note, even the possible transient decline may be avoidable with adequate carbohydrate intake[7] somewhere in the range of 30-60 gm of carbohydrate per hour during such exercise.[8]

Next, we can consider that regular aerobic exercise decreases the risk of chronic illnesses such as insulin resistance, cardiovascular disease, neurologic decline, and tumor growth. The mechanism by which it does this is in part by decreasing the amount of the more dangerous visceral fat that is stored around the internal organs, which is in and of itself highly inflammatory.[3] However, there is some evidence that exercise also has direct anti-inflammatory effects. The mechanism, yet to be elucidated, may involve the following:

- Reduced accumulation of inflammatory cells in fat tissue
- Release of immune molecules that attenuate inflammation
- Stimulation of the parasympathetic (“rest and digest”) portion of the nervous system
- Improvement in ability of the individual’s body to adapt (i.e., exercise acts as a stressor to which the body can respond and improve its function)[9]

Exercise may have a role in cancer care as well. While further research is needed, there is some evidence that immune function in patients being treated for or with a history of cancer can affect rates of recurrence. Several studies of patients either going through chemotherapy or with a history of cancer show regular physical activity is associated with improvement in several cancer-specific immune components[10]. Exercise has shown to decrease the suppression of markers of innate immune cell function by intratumoral lactate levels.[11] Reduction in proinflammatory markers may be most significant when a combination of aerobic and resistance training is employed.[12] Overall, exercise has the potential to target tumor growth by supporting the function of cytotoxic immune cells and controlling acute and chronic inflammation. [13]

While the above studies focused on aerobic, moderate-intensity exercise, other forms of movement benefit immune function. There is evidence that qi gong, tai chi, and yoga practices, which involve intentional meditative movement and breathing, improve immune function through a variety of immune pathways.[14-16] A recent review of 15 randomized control trials (RCTs) that looked at the impact of yoga on various markers of immune function found that regular yoga practice can downregulate proinflammatory markers such as IL-6 and TNF-alpha.[17] This may be particularly important for those with physical conditions that preclude more-intense exercise regimens.

Working the body can have a significant influence on immune function for many different illnesses, and beneficial approaches include tai chi, qi gong, and yoga, as well as aerobic, moderate-intensity exercise.

Surroundings

Environmental exposures can clearly influence immune function. Certainly, those with environmental allergies such as dust mites or pet dander do much better with avoidance of those allergens. For those individuals, allergy testing with an allergy specialist may make sense. However, there are a number of common chemicals, which are nearly omnipresent, that have been found to negatively impact immune function as well—potentially even leading to imbalances of the immune system, predisposing us to higher levels of autoimmune diseases such as allergies and asthma.[18] Perfluorinated compounds (PFCs) are chemicals found in nonstick pans, furniture, cosmetics, household cleaners, clothing, and packaged food containers. Dioxins are by-products of paper manufacturing and in the combustion of many different forms of waste that are extremely persistent and widely found in the environment due to atmospheric dispersion, deposition, and subsequent accumulation in the food chain. They have been found in soil, sediment, fish, meat, cow's milk, human fat tissue and breast milk. Both of these chemical classes have been found, in addition to other adverse health effects, to suppress immune function,[19] as has long-term exposure to particulate matter in the air.[20] These are only a few examples of chemical pollutants—there are tens of thousands more which have unproven safety profiles.

Becoming more aware of the number of chemicals to which we are exposed and their potential for negative impact on our health can be overwhelming. When working with individuals on this aspect of environmental health, it is prudent to focus on what *can* be controlled—i.e., limiting exposures using resources such as the website of the Environmental Working Group and supporting overall health so that the body's inherent detoxification mechanisms can operate optimally.

Personal Development

Stress in general has been found to have an impact on many aspects of physical and emotional health, even to the point of decreasing the antibody response to immunization with influenza vaccines.[21] Job stress (such as high demands, low control, high strain, job dissatisfaction, effort-reward imbalance, over-commitment, burnout, unemployment, downsizing, recessions, etc.) has been found to reduce a variety of immune functions while increasing inflammatory markers.[22] The studies looking at this were challenged by the sheer number of economic, psychosocial, and comorbid medical issues that influence job (or lack of employment) related

stress. However, because employment is both a source of income that is required to support our basic needs and many times a large part of how we see ourselves and/or contribute to society, it is important to understand how work affects the health of individuals.

As mentioned above, inflammation is a large part of the pathophysiology of many chronic diseases, including asthma. Asthma symptoms are more likely to flare in the face of psychosocial stress such as low socioeconomic status and urban living. Immune changes with stress-induced flares may actually make the individual less responsive to the corticosteroids used to treat that exacerbation.[23] Therefore, despite appropriate medication regimens, it may not be possible to control asthma adequately without addressing emotional stressors. It would not be a stretch to see this applying to other chronic diseases as well.

Nutrition

Let food be thy medicine and medicine be thy food.

—Hippocrates

Nutrition may be the single, most-important factor in optimizing immune function and controlling inflammation in the body because it can have a positive or negative impact depending on dietary patterns. The food we eat can be broken down roughly into micronutrients (vitamins and minerals, which are only required in small amounts) and macronutrients (protein, carbohydrate, and fats).

A large number of micronutrients have been studied in terms of their impact on immune function. The following is a summary of some of the more recent data on several important immune-mediating micronutrients.

Vitamin A

Vitamin A deficiency has been linked to decreased function of both innate and adaptive immune cells, leading to increased susceptibility to infections. Supplementation in deficient children has been shown to decrease morbidity and mortality from infectious diseases.[24]

Note that supplements containing vitamin A might put individuals at risk for toxicity. Therefore, supplements should contain beta-carotene or other provitamin A carotenoids that the body can then convert to the active vitamin as needed. The recommended daily allowances (RDA) for vitamin A are given as retinol activity equivalents (RAE). For adult men, this is 900 mcg RAE, and for women, 700 mcg RAE. Dietary sources of vitamin A include liver, sweet potatoes, spinach, pumpkin, and carrots.[25]

Vitamin B6

Deficiency of vitamin B6 can lead to low white blood cell counts, decreased innate immune function, and lowered antibody response to antigens.[24] Note that excess vitamin B6 supplementation can result in severe and progressive sensory neuropathy characterized by loss of control of bodily movements. The RDA of vitamin B6 is 100 mg per day for adults. Dietary sources of vitamin B6 include chickpeas, liver, tuna, salmon, chicken breast, fortified cereals, and potatoes.[26]

Vitamin B12 and Folate (formerly known as Vitamin B9)
Vitamin B12 deficiency, in addition to leading to macrocytic anemia and paresthesias, can contribute to depressed immune responses such as decreased T cell proliferation. Deficiencies in folate manifest similarly to those of B12—macrocytic anemia and depressed immune response.[24]

Vitamin C
Vitamin C plays an important role in many aspects of the innate and adaptive immune systems and acts as a potent antioxidant. Vitamin C deficiency results in higher susceptibility to infections. Vitamin C deficiency can also lead to increased oxidative damage and severity of infection (especially of the lower respiratory tract), decreased resistance to infection and cancer, and impaired wound healing. Supplementation may protect immune cells from oxidative stress, reduce incidence and duration of pneumonia in older people, and reduce duration and severity of respiratory infections, diarrhea, and malaria in children. Vitamin C demand rises during acute infections due to increased metabolic requirement. Doses required to saturate plasma levels and optimize cell and tissue levels in order to prevent infection are somewhere in the realm of 100-200 mg/day. [24]

Vitamin C is one of the few specific therapies used to treat patients with COVID 19, the illness caused by the novel coronavirus, which seems to have originated in Wuhan, China in late 2019 and caused a worldwide pandemic. Intravenous vitamin C seems to have a potent anti-inflammatory effect in the lungs and may help mitigate some of the significant pulmonary damage caused by this virus in critically ill individuals, although this requires more data to determine timing and required dosing. [27]

Foods rich in vitamin C include citrus fruits, tomatoes, potatoes, red and green peppers, kiwifruit, broccoli, strawberries, Brussels sprouts, and cantaloupe.[28]

Vitamin D
Vitamin D deficiency has been associated with increased susceptibility to infections (especially of the respiratory tract), increased severity of infections, reduced mass of immune system organs and cells, and increased risk of autoimmune diseases. It also has been implicated in increased susceptibility to and poorer immune function in HIV infection. Through activation of the nuclear vitamin D receptor (VDR) and the vitamin D metabolizing enzymes (both of which are present in nearly all immune system cells), vitamin D has significant immunomodulatory effects in essentially all aspects of the immune system. When deficient, supplementation has been shown to decrease respiratory tract infections. However, supplementation in vitamin D sufficient individuals is of unclear value and the data for benefit on disease risk and severity is hopeful but far from complete.[24,29,30]

Higher levels of 25-hydroxy-vitamin D have been associated with improved survival in colorectal cancer (CRC) patients, both pre- and post-diagnosis. Vitamin D is a modulator of both the innate and adaptive immune response and exerts a range of anticancer effects including anti-proliferation, induction of differentiation, induction of apoptosis, suppression of angiogenesis and anti-inflammation.[11]

The RDA for vitamin D is between 600 and 800 IUs daily for adults (15-20 mcg). However, given that a major source of vitamin D is exposure to sunlight, deficiency is not uncommon in latitudes farther from the equator. Serum levels of 25-hydroxyvitamin D [25(OH)D] of less than 20 ng/mL are considered deficient but many labs indicate <30 as being "low." It is reasonable to alter supplementation dose in order to maintain a level above 30. While risks of vitamin D toxicity are relatively low, levels >60 ng/mL may have some adverse effects.[31]

Vitamin E

While vitamin E deficiency is rare, when present, it negatively affects function of both innate and adaptive immune responses. Supplementation has been linked to decreased respiratory tract infections in older people.[24] The RDA for vitamin E is 15 mg daily. Vitamin E is best obtained through food; rich dietary sources include nut oils, sunflower seeds, almonds, hazelnuts, and peanuts.[32] If dietary supplements are used, look for products that contain mixed tocopherols.

Copper

Deficiency in copper can lower numbers of neutrophils, which are key players in the innate immune response. Supplementation can be beneficial to immune function in those who are deficient but over supplementation has been shown in some subsets of humans to decrease the antibody response to the influenza vaccine.[24] The RDA for copper is about 900 mcg and dietary sources include shellfish, seeds and nuts, organ meats, wheat-bran cereals, whole-grain products, and chocolate.[33]

Iron

Iron deficiency can lower the capacity of the immune system to mount an adequate response to infection. However, over-supplementation can result in organ damage and may actually provide a growth advantage to pathogens.[24] The RDA for adult males and postmenopausal females is 8 mg, and 18mg for menstruating adult females. Heme iron is more readily absorbed than non-heme iron. Heme iron is rich in lean meats and seafood, while non heme iron is found in nuts, beans, vegetables, and fortified grain products.[34] Concomitantly consuming a source of vitamin C increases iron absorption.

Selenium

Deficiency in selenium can impair innate and adaptive immune responses, increase virulence of viral infections and increase cancer incidence. While supplementation in deficient individuals may improve immune function, caution must be taken given the possible risk of worsening allergic asthma symptoms and decreasing the immune response against parasitic infections.[24] The RDA for selenium is 55 mcg. Dietary sources include Brazil nuts, seafoods, organ meats, muscle meats, cereals and other grains, and dairy products.[35]

Zinc

When there are disruptions in zinc metabolism, aspects of immune function are impaired including maturation and function of lymphocytes in the adaptive immune response, innate immune reactions such as phagocytosis and oxidative bursts and communication between components of the immune system through cytokines.[36] Zinc also acts as an important regulator of the immune response and anti-inflammatory agent. In chronic zinc deficiency, levels of proinflammatory cytokines increase leading to potential increased risk and severity of chronic inflammatory diseases (e.g., rheumatoid arthritis).[37] Zinc acts as a gatekeeper of the

immune system. While deficiency can lead to overproduction of inflammatory molecules, atrophy of the thymus gland, disruption in the balance of T cells and decreased numbers of certain types of B cells, excess zinc can suppress the function of B and T cells and directly activate other inflammatory cells. [38]

Zinc deficiency has been linked to increased bacterial, viral, and fungal infections as well as increased atrophy of the thymus. Supplementation with zinc has been shown to restore function of the thymus and improve immune function in the setting of gastrointestinal and respiratory tract infections, and reduce overactivity of cells types implicated in autoimmunity.[24] The RDA for zinc is 11 mg for adult males and 8 mg for adult females. Oysters are especially rich in zinc, but red meat and poultry also offer zinc, in high amounts. Other sources include beans, nuts, certain types of seafood (such as crab and lobster), whole grains, fortified breakfast cereals, and dairy products.[39]

We are also discovering more and more that the impact of what we eat is not simply about the combination of micronutrients and macronutrients. Our nutrition patterns, in addition to other lifestyle habits, greatly influence the environment of the digestive tract (which is the major interface between the external world and our internal environment) and the incredibly important mix of bacteria that reside there—the "microbiome." This microbiome has powerful influences on metabolism, disease risk, mood, and cognitive function. The significance of the microbiome is illustrated in a study in which the transfer of a sample of a lean person's intestinal bacteria to the gut of an individual with metabolic syndrome (a sort of prediabetic state) resulted in significant increase in insulin sensitivity of the receiver.[40] Of note, the microbiome of the skin also increasingly is recognized as an important part of the health of skin and its immune system and of the pathology of skin diseases.[41]

The Microbiome

The microbiome of the GI tract has a huge regulatory impact on our immune function—not only protecting us from illness-causing microbes but possibly also preventing the overactivity of the immune system seen in autoimmune diseases such as food allergies. Disruptions in the gut microbiotia ("intestinal dysbiosis") have been implicated in several autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, and myasthenia gravis. While genetic and environmental factors certainly also play significant roles, certain gut bacteria patterns have been associated with these diseases and therapeutic interventions to shift those patterns have shown some improvement in disease expression. [42]

The balance of the human intestinal microbiome is influenced heavily during birth and in the newborn period. The meconium of full-term newborns contains bacteria normally found in the maternal amniotic fluid, vaginal canal, and oral cavity. Infants born via cesarean section have a different composition of their intestinal microbiome that bears more resemblance to skin bacteria. Components of human breast milk act as prebiotics to help foster growth of healthy bacteria and antibiotics against pathogenic bacteria. This combined with the fact that breast milk also contains 10^9 bacterial cells/L indicates how breastfeeding infants helps to support the growth of helpful bacteria such as *Bifidobacterium* spp. and *Lactobacillus* spp. As the GI tract develops, the gut microbiome has significant impact on its maturation and on the training of the large portion of the immune system that resides in that GI tract. The commensal bacteria help train the gut immune system to tolerate healthy bacteria, which prevents problematic chronic

inflammation, and also stimulate the immune system at a low level to be able to recognize and fight pathogenic bacteria. There also seems to be a window in early life in which the constitution of the gut microbiome influences overall stress responsiveness and anxiety. Supplementation with a probiotic may have a greater impact on immune function in older adults.[43]

Older adults are more susceptible to infections and cancer, which in turn are associated with a decrease in cellular immunity. A meta-analysis of several small studies found that supplementation with a specific strain of bacteria (*Bifidobacterium animalis* ssp *lactis* HN019) improved markers of cellular immune function including enhanced natural killer cell tumoricidal activity and polymorphonuclear cell phagocytic capacity.[44]

Prebiotics are nondigestible food ingredients that help support good bacteria in the gut; examples include fructo-oligosaccharides, lactulose, lactitol and gluco-oligosaccharides. Generally, they are not digested until they get to the large intestine. Foods rich in prebiotics include honey, beer, onions, burdock root, asparagus, rye, Jerusalem artichokes, bananas, maple sugar, oats, and Chinese chives.[45] The role of prebiotics supporting gut health through reducing pathogens and improving the balance of pro- and anti-inflammatory cytokines has mostly been studied indirectly by looking at how they support the growth of healthy bacteria, but more is being learned about their direct effects on gut health and immunity as well. [46]

Probiotics act directly on the health of the gastrointestinal tract by increasing the activity of natural killer cells and macrophages and influencing the secretion of immunoglobulins and cytokines. They act indirectly by enhancing the gut epithelial barrier, altering mucus secretion and competitively excluding pathologic organisms. Different bacterial strains accomplish these influences via different mechanisms and knowing what type, when, and how much probiotic to supplement for any given disease state or cause of dysbiosis is an active area of study.[47]

What it takes to keep the gut healthy may vary based on the individual. However, a few key components are rather common to all:

- Avoidance of excess amount of inflammation, which can be caused by foods and medications that irritate the gut and/or lack of effective mechanisms to deal with life's stresses
- A healthy mucous layer, which lubricates the intestinal lining and feeds the healthy bacteria that reside there
- An appropriate mix of healthy bacteria

For more information, See the "Irritable Bowel Syndrome (IBS)" Integrative Health tool.

General principles around healthy eating were summarized well by Michael Pollan in his book *In Defense of Food*, in which he advised, "Eat food. Not too much. Mostly plants." Many of us may be looking for miracle foods that will boost immunity. Coffee has been linked to lower levels of circulating chemokines and cytokines and increased diversity of the gut microbiota. [11] Garlic has been shown to increase macrophage activity, natural killer cells and the production of B and T cells in addition to decreasing the number, duration, and severity of upper respiratory infections. It appears to have antiviral actions against human rhinovirus, cytomegalovirus,

herpes simplex, and influenza, in addition to antifungal and antiparasitic activity against organisms such as *Candida albicans*, *Cryptosporidium,* and *Giardia*. In addition to in vitro studies, trials have used garlic powder and aged garlic extract to show decrease in upper respiratory infections. As a whole food, garlic also acts as a prebiotic that helps support a healthy microbiome.[48] In most cases, eating an anti-inflammatory diet can accomplish the adequate intake of the above micronutrients and foster a supportive environment for healthy gut bacteria. See "The Anti-Inflammatory Lifestyle" handout for more information.

Moderation of caloric intake also is important. Studies have shown that undernutrition of macronutrients leads to more-frequent chronic infections but macronutrient excess has been associated with induction of inflammation and increased risk of chronic diseases such as diabetes and heart disease.[49]

Anti-inflammatory diets are generally high in fiber as well. Diets higher in fiber have been shown to decrease colorectal cancer (CRC) incidence, and improve prognosis if CRC is diagnosed. Gut bacteria can ferment insoluble fiber to produce short-chain fatty acids, which have beneficial effects on the gut immune system and protection against CRC.[11]

Traditional plant-based diets such as the Ancient *Thali* diet of India, heavily influenced by tenets of the Indian medicine Ayurveda, has been shown to be associated with lower rates of chronic disease such as type 2 diabetes and colon cancer. This diet is low in processed foods, rich in prebiotic fiber and in plants and spices, which contain a wide variety of bioactive compounds that are anti-inflammatory in nature and help promote a healthy gut microbiome. An example of these compounds is anthocyanins, a class of phytochemicals called polyphenols that are abundant in dark-colored fruits and vegetables such as berries, eggplants, and other red, purple, and blue produce.[50] Flavonoids are another category of polyphenols. A recent meta-analysis of 14 studies showed that supplementation with dietary flavonoids (0.2 to 1.2g/day) may decrease incidence of upper respiratory tract infections by 33% and decrease sick day counts by 40%. [51]

The balance between omega-6 and omega-3 polyunsaturated fatty acids (PUFAs) in our diets is of particular importance. The same enzymes in the body metabolize both, but the omega-6 fats promote inflammation while omega-3 fats promote wound healing and resolution of inflammation.[49] Higher levels of marine-based omega-3 fatty acid intake has been shown to decrease recurrence and mortality rates in CRC. This seems related to both the immune-modulating effects and beneficial impact on the gut microbiota of omega-3 fatty acids. [11]

Beneficial impact of omega-3 fatty acids on the arachidonic acid to EPA ratio in cell membranes may be greater in older adults. [43]

Addition of omega-3 fatty acids to parenteral nutrition given in the post-operative period of patients with gastrointestinal cancers results in a more favorable immune function profile and decreased risk of infective complications.[52]

The ideal ratio of intake of omega-6 and omega-3 fats seems to be around 2:1, but the standard American diet contains a ratio of something like 10:1 to 25:1—strongly tipping the balance toward inflammation. In general, an anti-inflammatory diet includes the following foods:

- Cold water fish, flax, and nuts
- A wide variety of fruits and vegetables of various deep colors
- Whole grains
- Anti-inflammatory spices such as turmeric, ginger, rosemary, oregano, and cayenne

An anti-inflammatory diet avoids or limits the following foods:

- Foods high in trans- and omega-6 fats (processed and red meats; dairy; partially hydrogenated oils; corn, cottonseed, grapeseed, peanut, and soy oils)
- Refined carbohydrates (white breads, instant or white rice, rice and corn cereals, crackers, cookies, cake, etc.)
- Soda and juices[53]

In animal models, poor parenteral nutrition patterns negatively affect immune function regardless of the diets of the offspring. [54]

A large number of herbal and nutritional supplements have been studied for their role in optimizing immune function. The list and discussion on that topic is beyond the scope of this overview but is discussed in the "Adaptogens" tool.

Never underestimate the power of diet when it comes to treating inflammation and bolstering the immune system. The anti-inflammatory diet is one of the most popular tools used by integrative medicine practitioners.

Recharge

Numerous studies outline the relationship between sleep and immune function. Many of these have found a correlation between changes in markers of innate immunity, such as interleukin 6 and tumor necrosis factor alpha levels, and sleep disruption. [55] Both sleep deprivation and acute illness (such as a viral infection) increase inflammatory markers that have been found to make us more tired. Reciprocally, sleep deprivation leads to decreased immune function, leading to increased frequency of infections and decreased response to immunizations such as the influenza vaccine. Increased levels of inflammation result from sleep deprivation, which may be the mechanism by which a chronically inadequate amount of sleep is associated with malignancy, heart disease, and stroke.

In contrast, sleep strengthens the immune response—most immune cells' response to challenges (e.g., viral infections) peak at night. These factors become a significant disadvantage for shift workers who have higher rates of gastrointestinal disease, cardiovascular disease, diabetes, metabolic syndrome, and cancers including prostate, colorectal, endometrial, and breast.[56] Adequate sleep appears to be 7-8 hours per night. Too much sleep (greater than 10 hours), however, has been associated with increased risk of cardiovascular disease.[57] The body seems to have evolved with a basic sleep requirement for optimal immune function, and the importance of regular, adequate sleep should not be underestimated as it relates to both short-term immunity and long-term chronic disease risk. Interventions such as tai chi and Cognitive Behavioral Therapy for Insomnia (CBT-I) have been found to improve sleep and lower inflammatory markers significantly compared to controls such as attending a sleep seminar.[55]

This speaks to the importance of active participation of the individual in improving their personal health outcomes.

Family, Friends, & Co-Workers

An interesting study took 90 newlywed couples and monitored several measures of immune function after a 30-minute discussion aimed at addressing and attempting to resolve 2-3 marital issues that pre-discussion questionnaires deemed to be the most likely to induce conflict. Subjects, especially women, who showed more negative or hostile behaviors during the discussion were more likely to show decreases on several markers of immune function.[58] How we perceive or handle stress and conflict can influence the physical function of our bodies.

Stresses such as marital disruption and caregiving for a relative with Alzheimer's disease have been associated with both decreased in vitro function of immune cells and qualitative immune function changes such as frequency of herpes outbreaks. There is some evidence to suggest that *quality* interpersonal relationships can be protective against these types of immune changes.[59] Indeed, higher levels of social support have been shown to improve multiple aspects of immune function, including changes in CD4+ cell counts (a marker of HIV disease progression) in HIV-positive individuals.[60]

- Personal relationships do not have to be limited to friends and family. David Rakel et al. performed an interesting study looking at the influence of a physician's empathy on the outcomes of the common cold. About 350 individuals were randomized to receive either: Standard care for cold symptoms in which the clinician took adequate history and performed appropriate physical exam, but avoided any attempt to connect with the patient or express empathy for their discomfort, or
- "Enhanced" care in which the clinician strived to connect with the patient as an individual and offer compassion and empowerment to the patient for self-care.

Quantitative measures of immune response trended toward more robust, and symptom severity trended toward less severe in the enhanced group, but neither was statistically significant. However, the duration of the illness was a full day less in those who felt a connection with or empathy from their clinician—this was statistically significant and comparable to the effects of the few antiviral medications that have been studied.[61] The clinicians' presence and compassion make a difference—human connection makes a difference.

Stress reduction should be a key component of any health plan where inflammation and supporting the immune system require attention.

Spirit & Soul and Mind & Emotions

Individuals with higher levels of spiritual well-being, including participation in formal religion, seem to have better cardiovascular, neuroendocrine, and immune function.[62] [63] In our practice we frequently ask about spirituality, but we make sure that patients understand we are asking *them* how they define that. Some helpful phrases that can start this conversation include the following:

- "What do you feel connects you to things or people outside yourself?"
- "What gives you a sense of meaning or purpose?"

- "What makes you get out of bed in the morning?"

To help avoid people feeling like we are just asking about religion, we sometimes offer examples such as, "For some it is religion or meditation, but for others it is nature, music, the meaning of their work, art, being present with friends and family, volunteer work, etc."

When our lives encounter a challenging time (e.g., stressed interpersonal relationships, illness in ourselves or in family members, etc.), our reactions to those situations can affect our resiliency and immune function. For example, a review of 15 published trials showed eight that indicated psychotherapy improved cancer survival time and none showed an adverse effect. While the mechanism of this result has yet to be elucidated, it is likely related to the relationship between stress and immune dysfunction, increase in inflammation, increase in stress hormones and/or changes in DNA and DNA expression related to these factors.[64]

Mindful awareness meditation has been studied extensively in relation to immune function. This type of meditation is a practice that fosters an ability to take a step back and notice our reactions to external stimuli, giving us a chance to pause and choose how we will respond. My favorite analogy to understand this was given by Katherine Bonus—former director of the University of Wisconsin Mindfulness-Based Stress Reduction Program. She had a group of us look out a window at the street. She told us to imagine just flinging ourselves on top of the next car that drove past—being carried away on top with no idea where it would take us or how fast or when it will turn. This was a lot like how we might react to stress or pain—we see it coming and feel it is going to do something to us or cause us to feel a certain way, and we let it. If we stop and observe exactly what it is, without expectation, we may have a bit of a decision point on how to respond differently. Do I have to let that stress me out? Is the pain really that bad, or am I expecting it to be? And so on.

Some studies have shown mindful awareness to lead to more robust antibody response to the influenza vaccine.[65] Others have failed to show this relationship but did correlate optimism, less anxiety, and lower perceived stress with high antibody levels post-immunization[66] Mindful awareness meditation has been associated with decreased symptom severity in the common cold.[67] Immune function profiles shifted from depressed to more normal profiles in patients with breast and prostate cancer after completion of an eight-week Mindfulness-Based Stress Reduction (MBSR) course.[68] In women with breast cancer, mindful awareness has been shown to improve the cytotoxic activity of natural killer cells, which can be suppressed in the disease process.[69] A review of randomized control studies found that mindful awareness meditation decreased inflammation (as evidenced by decreased NF-kB transcription activity and CRP levels), increased cell-mediated immunity (as evidenced by increased CD4+ cell count/activity), and slowed biological aging (as evidenced by increased telomerase activity).[70]

Some believe meditative practices can positively impact cardiovascular health through the anti-inflammatory reflex.[71] MBSR has been found to decrease markers of post-stress inflammation that may have implications for its use in chronic inflammatory conditions.[72] Some evidence supports use of workplace-based mindful awareness programs as a means of decreasing inflammation as measured by decreases in CRP (a common marker of generalized inflammation), especially in nonobese individuals.[73]

Mechanisms by which mindful awareness impacts immune function likely have to do with the connection between emotional states, neurologic function, and the immune system. This field of study, psychoneuroimmunology, is growing and seems to be scratching the surface of how our perception of the world impacts our physiology. There appears to be a bidirectional relationship between the psychosocial impact on immune function and health of the immune system on resilience of an individual when confronted with both biologic and social challenges.[74] Mindful practices are not limited to meditation, however. It is important to recognize that meditation may be counter to the belief systems of some individuals or simply not appealing to them. Other examples of mindful practice are mindful walking, listening to music with two instruments and following just one, painting, working with one's hands, and breathwork. For more information, see the "Mindful Awareness" and "Mind and Emotions" Integrative Health tools.

Personal Health Plan

Name: Joanne

Mission, Aspiration, Purpose (MAP):

My mission is to feel like a strong, healthy individual who is a good example of health for his children.

My Goals:

- Quit smoking.
- Improve ability to get to sleep.
- Improve understanding and control of asthma.
- Find ways to become less susceptible to frequent minor infections.
- Increase fitness to the point of being able to participate in longer road bike races.
- Find a healthy way to deal with the health problems of my brother and father.

Areas of Self-Care:

- Physical Activity
  - Progressively increase biking mileage after consulting with doctor about asthma. Get connected with a local bicycling club to help train for longer rides.

- Surroundings
  - Continue smoke cessation.
  - Medically, make sure nothing is triggering asthma symptoms. Consult a doctor and together decide if there is an allergic component that would benefit from either medication or allergy testing. Think about the air quality at home and work and regularly change furnace filter or bring an air filter to the office.
  - Bring a few personal things into the office space to give the space a nicer feel.
  - Minimize unfinished reminders at home. Keep the workspace for current projects limited and organized. Reframe the next project as "possibility" rather than something stressful.

- Nutrition

- Follow an anti-inflammatory diet to get more energy and help the immune system function at its peak. Decrease or cut out fast food and try to incorporate more fruits and vegetables—the more different colors, the better.

- Recharge
  - Sit down with my wife, list all of the projects, and give a reasonable timeline—considering all other priorities. Make a to-do list and leave it outside the bedroom door the night before a busy day. Consider breathing exercises or a progressive muscle relaxation activity to help fall sleep.

- Spirt and Soul/Mind and Emotions
  - Start with things mentioned above and reflect on how they affect my overall sense of contentment by meditating or journaling. Commit to thinking of 2-3 things each day for which I am grateful—opportunities, relationships, material things, etc. Consider doing this as a family at the dinner table or with my kids when tucking them in.

- Personal Development/Family, Friends, and Co-Workers
  - Reframe the way I think about work. In sales, easing that process for clients has the potential to make their day easier. There is a potential for purpose with every human interaction. Try to connect with co-workers once a month—attend a planned get-together or just strike up a conversation in the break room.
  - Carve time out each week to do an activity with my wife and children that is simply fun. Give everyone a turn in picking the activity—movie night, hiking, bowling, etc.
  - Read "*Anticancer: A New Way of Life*," by David Servan-Schreiber, an empowering book that may help me reflect on my personal cancer risk from my father.
  - Look into Al-Anon—a support group for people with friends and family with drinking problems—to support my brother. Offer support for his wife and children as well.
  - Volunteer at my children's school to build a garden shed to give me something meaningful to do, while also getting to know others who may want to help.

Professional Care: Conventional and Complementary

- Prevention/Screening
  - Meet with primary care physician for complete review of health.

- Treatment (e.g., conventional and complementary approaches, medications, and supplements)
  - Prescription medications
  - Astragalus 5-6 gm per day
    - Can help prevent the common cold and take seasonally as needed. Look for a label that has a USP or GMP seal to ensure a quality product.
  - Omega-3 fatty acids or fish oil 1,000 mg of DHA + EPA
    - Look for a product that is molecularly distilled to remove metals like mercury.

- Skill building and education
  - Sleep hygiene
  - Nutrition
  - Foster a connection, sense of purpose, and gratitude

Referrals/Consults

- Allergist

Community

Resources

- Removing chemicals leaves less “stuff” for the immune system to deal with; visit the Environmental Working Group for more information.

My Support Team

- Primary Care Clinician
- Wife and kids

Follow-Up with Joanne

Through the process of completing his Personal Health Inventory (PHI), Joanne realized that her life did not offer her the enjoyment he would like to have. She felt sick all the time and was, to some degree, nervous about going forward with more exercise for fear of making her asthma worse. She did not feel all that connected to anyone outside of he immediate family and had some significant stress with the health of her brother and father. She wanted to do something with meaning, as her job was mostly a reliable source of income. She desired to feel strong and healthy and be a good role model for her children.

Joanne decided to start out by scheduling an appointment with her doctor to follow up regarding her asthma. She wrote down a list of questions so that she would have a clear understanding of what she should expect from his treatment plan and how she could better manage it at home. She also wanted to be clear on whether or not she had “restrictions” in terms of exercise. She also decided to commit to giving up smoking and to ask for some help in developing a plan for that. This became especially important as she realized its impact on her asthma and her worry given her father’s recent diagnosis of lung cancer. Given the limited number of cigarettes she smoked, she was able to quit in about a month. She felt he had a much better understanding of her asthma and knew when she needed to be seen due to symptoms.

Joanne also decided become more involved in her community. She felt volunteering to help her children’s school build a shed for their garden tools would be a good way to meet people. It was a setting that felt more comfortable, without the pressure of having to come up with conversation at a dinner party or other social event of that nature. She even asked another parent who she knew was in bicycling club if he wanted to help on the project as well. Joanne eventually joined that biking group and was able to participate in the 112-mile bike ride after steadily increasing her miles over about 2 years.

To help with her sleep, she decided to sit down with her wife and develop a time line of all the projects in the house that they want to do. They made sure it was over a long enough time frame and in small enough pieces that they could see progress without unreasonable expectations. With that plan, she was able to feel like he could start working at a reasonable time, relax a bit, and not have her mind planning things when she was trying to sleep.

Integrative Health Tools

- Adaptogens
- Allergies
- Asthma
- Herpes Simplex Virus (HSV) 1 & 2 Infection
- Prevention and Symptomatic Treatment of Viral Upper Respiratory Infections
- Sinusitis
- Urinary Tract Infections

Resources

- Environmental Working Group
- *Anticancer: A New Way of Life* by David Servan-Schreiber (2009)
- University of Wisconsin—Madison Integrative Health Program

Author(s)

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