THE COVID-19 Pandemic

Overview and Integrative Health Approaches

■ *Stephanie Maxine Ross, MHD, MS, HT, CNC, PDMT*

Holist Nurs Pract 2020;34(4):252–258

SARS-CoV-2 coronavirus is a newly emergent virus that is extremely virulent and highly contagious, with a global impact relative to the 1918 H1N1 influenza pandemic. Coronaviruses belong to the Coronaviridae family of viruses that can cause illnesses ranging widely in severity. The taxonomic classification of coronaviruses is complex because there are specific names for almost every virus within a species due to the long-standing perception that viruses are causative agents of specific diseases in specific hosts.[1] In addition, the formal system of nomenclature is used to classify newly discovered viruses that increasingly include viruses that have not been associated with any known viral disease in their respective hosts. If a virus prototypes a new species, it is regarded taxonomically as "novel." Upon an initial viral outbreak, it is extremely important to quickly establish whether the pathogen is caused by a new or previously known virus, since it helps determine which approach and specific actions are most appropriate to detect the causative agent, control its transmission, and limit potential consequences of the epidemic.[2]

> **"In three words I can sum up everything I've learned about life: it goes on."**
>
> **Robert Frost**

CORONAVIRUS PANDEMICS

Viruses that belong to the Coronaviridae family are characterized by an enveloped, single-strand, positive-sense RNA genome of approximately 30 kb in length.[3] Coronaviruses have been identified in several avian hosts, as well as in mammals, including bats, dogs, and cats. Although several coronaviruses are pathogenic to humans, most are associated with mild clinical symptoms,[3] with the exception of 2 large-scale pandemics that occurred in the past 2 decades. The first known severe illness caused by the coronavirus originated with the severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV) epidemic in Guangdong, China, in November, 2002,[4] and resulted in more than 8000 human infections and 774 deaths in 37 countries during 2002-2003.[5] The second outbreak of severe illness began in 2012 in Saudi Arabia with the Middle East respiratory syndrome (MERS) coronavirus (MERS-CoV) and resulted in 2494 cases and 858 deaths.[6] Although SARS-like coronaviruses have been widely identified in certain mammals including bats since 2005 in China,[7-10] the exact origin of human-infected coronaviruses remains unclear. More recently, the identification of multiple SARS-like coronaviruses found in bats points to these animals as probable hosts for natural reservoirs of these viruses.[11,12]

Author Affiliation: College of Nursing and Health Professions, Drexel University, Philadelphia, Pennsylvania.

The author has disclosed that she has no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

Correspondence: Stephanie Maxine Ross, MHD, MS, HT, CNC, PDMT, Associate Editor, Director, and Clinical Assistant Professor, Advanced Study in Complementary and Integrative Health Programs, College of Nursing and Health Professions, Drexel University, Three Pkwy, 9th Floor, Ste 9109, Philadelphia, PA 19102 (smr49@drexel.edu).

DOI: 10.1097/HNP.0000000000000398

COVID-19 (SARS-COV-2 CORONAVIRUS)

Proximal origin of SARS-COV-2

A new coronavirus associated with severe acute human respiratory disease emerged from China between mid-November and early December of 2019. Understanding the origin of a disease, how the disease spread, and determining how undetected and undocumented cases contribute to its transmission greatly improves the understanding of the magnitude of that threat. Epidemiological investigations have indicated that the outbreak originated in Wuhan, Hubei Province, central China.[13] The first known infected patient who presented with viral pneumonia due to an unidentified microbial agent was hospitalized in the Central Hospital of Wuhan on December 12, 2019, 6 days after the onset of disease.[13] The patient reported chest tightness, fever, a dry cough, and weakness for 1 week prior to admittance. A novel coronavirus was subsequently identified as the causative pathogen, and the Coronaviridae Study Group of the International Committee on Taxonomy of Viruses designated the virus as SARS-CoV-2 SARS-related coronavirus, a member of the genus *Betacoronavirus*, within the Coronaviridae family[14]; the World Health Organization determined the official name of the viral disease as COVID-19.[15] At the end of December, the Chinese authorities informed the World Health Organization of the SARS-CoV-2 coronavirus outbreak. Shortly after the epidemic began, the Chinese scientists sequenced the genome of SARS-CoV-2 and made the data available to researchers worldwide.

COVID-19 transmission[16]

The SARS-CoV-2 virus is highly contagious and spreads rapidly through close contact from person-to-person in respiratory droplets that are produced when an infected person coughs, sneezes, or talks. These droplets have the potential to enter through the mouth and nose of people in close proximity of the infected person and may contaminate nearby surface areas that act as transmitting agents. Individuals who are infected with the coronavirus often exhibit symptoms; however, recent studies suggest that COVID-19 may be spread by individuals who are asymptomatic. The efficiency of transmission for any respiratory virus has important ramifications for disease containment and mitigation strategies.

Although scientists worldwide are evaluating candidate therapies and vaccines to treat and prevent SARS-CoV-2 coronavirus infection, as of this writing there are no treatments or vaccines for COVID-19 that have been approved by the Food and Drug Administration (FDA). To date, the most effective method to prevent infection is to avoid exposure to the SARS-CoV-2 coronavirus. The Centers for Disease Control and Prevention has recommended strict guidelines for preventing the spread of COVID-19. These guidelines highlight the importance of maintaining a minimum 6 ft distance from other people, incorporating frequent "hand hygiene" with soap and water or the use of an alcohol-based hand sanitizer, wearing face masks, and the routine disinfection of frequently touched surfaces.

PATHOGENESIS OF SARS-COV-2

The immune response to different pathological invasions in the body is mediated by 2 types of system responses: an innate immune response and an acquired immune response.[17] Innate immunity provides the first line of immune response to viral infections. The function of the innate immune response is crucial because it serves to suppress viral replication and spread to other cells. It is also responsible for programming the adaptive immune response. The innate immune system is composed mainly of physical barriers, such as the skin and mucous membranes, chemical barriers, through the action of antimicrobial peptides and reactive oxygen species,[18] innate immune cells, and soluble mediators such as cytokines, chemokines, and the complement system, which provide protection in the initial phase of contact with pathogens and are responsible for preventing potentially harmful infections.[19]

The primary function of the innate immune system is (1) to prevent the entry of pathogens through physical and chemical barriers[18]; (2) to inhibit the spread of infection; (3) remove pathogens through the mechanisms of cytotoxicity and phagocytosis[20]; and (4) to activate the acquired immune systems.[21]

The innate immune system is the first line of immune response to viral infections. The antiviral response is initiated on detection of different viral antigens by pattern recognition receptors (PRRs) that detect pathogen-associated molecular patterns of the infected cell. The recognition of virus infection is

critical because it acts to suppress viral replication and spread to other cells at the early stages of infection.

Inflammation has always been associated with viral infections. The innate immune response to viruses consists of several main classes of PPRs, the most recently identified pathway in the recognition of RNA viruses is Nod (nucleotide oligomerization domain)-like receptors (NLRs). Nod-like receptor family, pyrin domain-containing 3 (NLRP3) is activated by various stimuli, including virus infections. These receptors recognize specific molecules found within the virus that are called PAMPs (pathogen associated molecular patterns) and cause subsequent activation of cytoplasmic NLRP3 inflammasomes.[22] The NLRP3 inflammasomes are multiprotein complexes that are made up of a sensor protein that is activated upon viral infection and triggers the release of proinflammatory cytokines specifically interleukin 1 beta (IL-1B) and interleukin 18 (IL-18), which play very important roles in antimicrobial host defense.[23] These proinflammatory cytokines induce a variety of immunomodulatory effects, capable of leading to both host protection and damaging pathological response in respiratory inflammation.[24]

Research has shown that inflammasome-regulated cytokines IL-18 and IL-1B are crucial mediators of lung injury, implicating the important role of the inflammasome pathway and its cytokines in respiratory inflammation.[24] As this relates to coronavirus infections, including SARS, MERS, and COVID-19, research has reported higher levels of IL-1B and IL-18 levels, not only in the blood of patients but also in lungs and lymphoid tissue, resulting in an acute inflammatory response that is symptomatic of the COVID-19 coronavirus.[25]

Continued research will provide a better understanding of the pathogenic mechanism of the SARS-CoV-2 coronavirus, which, in turn, will facilitate the development of effective interventions for both prevention and treatment.

INTEGRATIVE HEALTH STRATEGIES

The COVID-19 pandemic is an emerging, rapidly evolving global occurence.[26] Although scientists at the National Institutes of Health and in other countries are assessing potential therapies and vaccines to treat and prevent COVID-19, to date there are no treatments or vaccines for the novel coronavirus that have been approved by the FDA. Likewise, since SARS-CoV-2 is a novel coronavirus, there are no known integrative health agents that have been studied and validated in human trials as effective prevention or treatment therapies specific to the COVID-19 virus.[27] However, taking into consideration the known pathogenesis of the novel coronavirus, its characterizations within the Coronaviridae family, and its inflammatory nature, as well as the mental and emotional stress that has precipitated from the COVI-19 pandemic, there is existing supportive evidence of integrative health strategies that can be utilized as adjunctive therapies for supporting the mind, body, and spirit during these challenging times.

HEALTH-PROMOTING CONSIDERATIONS

The following integrative health considerations are intended to supplement the guidelines issued by the Centers for Disease Control and Prevention, which emphasize the importance of vigilant handwashing, social distancing, adherence to travel restrictions, protective masks, and, if disease symptoms should appear, contacting a health care provider.[28]

The first line of defense for any health-related condition is maintaining a strong immune system through the implementation of healthy dietary and lifestyle guidelines. This becomes even more important for individuals who suffer from illness, stress, and stress-related conditions.

ANTI-INFLAMMATORY EATING PLAN[29]

A health-promoting diet such as the "anti-inflammatory dietary plan" is rich in whole "natural," unprocessed food that is critical to support the biochemistry of the body and brain for optimal function and to lend increased resistance to both mental and physical stressors. The nutritional foundation for the anti-inflammatory diet provides optimum levels of all major nutrients, micronutrients, antioxidants, minerals, vitamins, and fiber that work together to help protect against inflammatory conditions and different types of stressors, while maintaining low levels of food components that are known to be detrimental to health such as refined carbohydrates, saturated fats, salt, cholesterol, and food additives.

The overall eating plan for an anti-inflammatory diet is exemplified in the traditional Mediterranean dietary plan,[29] which consists of fresh food sources, including vegetables, legumes, whole-grain cereals, fruit, nuts, and extra virgin olive oil (EVOO); moderate-to-high consumption of fish and poultry; and a relatively low consumption of red meat and dairy products that contributes synergistically to what has become known as a holistic prescription for good health and longevity.

Fruit and vegetables

A high intake of fresh fruit and vegetables has been shown to protect against many diseases due to their anti-inflammatory action. Vegetables provide the most extensive range of nutrients and phytochemicals, especially fiber and carotenes, of any food group. Fruit and vegetable antioxidants, including flavonoids and vitamins, have a potent anti-inflammatory effect. In addition, vegetables high in fiber play a critical role in the prevention of inflammation, since there is an inverse association between fiber intake and C-reactive protein (CRP). Studies show that a greater intake of fruit and vegetables is associated with lower CRP and homocysteine levels.

Flavonoids have potent anti-inflammatory properties and can be found in fresh fruit and vegetables, such as apples, blueberries, strawberries, cranberries, citrus fruits (oranges, tangerines, grapefruit, lemons, and limes), broccoli, spinach, watercress, kale, onions, and celery.

Extra virgin olive oil

Extra virgin olive oil is produced from the first pressing of the olive fruit through the cold-pressing extraction method and is the most valued form of olive oil for both its taste and health benefits because it maintains the integrity of the full spectrum of chemical constituents. The major chemical components of EVOO are glycerol fractions composing up to 90% to 99% of the olive fruit and unsaponifiable fractions containing phenolic compounds that make up to 0.4% to 0.5% of the olive fruit. Research studies have demonstrated that EVOO phenolic compounds are highly bioavailable in humans. The high bioavailability of these compounds lends support to the evidence that phenolic compounds have positive effects on certain physiological parameters such as plasma lipoproteins, oxidative stress, inflammatory markers, platelet and cellular function, antimicrobial activity, and bone health.

Whole grains

Whole grains are fundamentally the most important food crop in the world, literally the "staff of life," and provide one of the foundational food components in the Mediterranean diet. Grains contain a high content of nutrients that are related to beneficial health effects, such as vitamins E and B, minerals, antioxidants, and a wide range of phytochemicals that are associated with long-term health. The intake of whole grains, in particular whole-grain bread, is associated with a broad array of health benefits that include a decrease in cardiovascular disease, type 2 diabetes, and metabolic syndrome.

NUTRITIONAL SUPPLEMENT CONSIDERATIONS

A strong nutritional foundation is an important component in supporting emotional, mental, and physical health. There is increasing evidence that the appropriate use of nutritional supplementation when combined with high-quality food sources helps support optimal health. This is particularly evident when a person is experiencing excessive stress levels that can precipitate anxiety, depression, and stress-induced insomnia.

A basic nutritional supplement program includes a high-potency multiple vitamin and mineral formula, a full-spectrum antioxidant, and specific nutritional supplements to help potentiate immune function, such as vitamin C, zinc, and omega 3-fatty acids.

PHYTOMEDICINE CONSIDERATIONS

German chamomile

German chamomile (*Matricaria recutita*) is recognized as one of the world's most well-known medicinal plants and is used extensively for the treatment of a wide range of conditions due to its anti-inflammatory actions, such as stomach upset and ulcers to inflamed skin and mucous membranes, and notably for its relaxation and calming effect.

Chamomile is known for its broad-spectrum pharmacological actions, including its anti-inflammatory, analgesic, antispasmodic,

wound-healing, antimicrobial, and sedative properties. The principal bioactive phenolic compounds are found in the dried floral heads that consist of the flavonoids apigenin and quercetin, which are highly stable and water-soluble. Aqueous extracts, such as infusions (tea), are recommended by the German Commission E for its carminative effect and mild sedative action to reduce anxiety, calm nerves, and treat insomnia.[30]

Elderberry (*Sambucus nigra* var *canadensis*)

Elderberry is used primarily for the treatment of colds, influenza, feverish conditions, and for its immunostimulating effects. Elderberry fruit (berry) contains several active constituents that are rich in antioxidant and anti-inflammatory compounds, including flavonoids (quercetin), anthocyanins, and vitamins A and C. Clinical studies have found that elderberry extracts can inhibit influenza A and B infections, and preclinical studies have shown antiviral effects.[31] Research has demonstrated that flavonoids bind to the surface of the H1N1 influenza virus and interfere with host cell receptor recognition and/or binding.

Green tea (*Camellia sinensis*)

Green tea polyphenols are one of the most potent antioxidants known. The buds and leaves of green tea contain active constituents that consist of catechins, in particular epicatechin (EC), epigallocatechin (EGC), and epigallocatechin gallate (EGCG). Catechins make up as much as 30% of the dry weight of green tea buds and leaves and have clearly demonstrated greater antioxidant protection than vitamins C and E. In addition to its direct antioxidant activity, the catechins in green tea have anticancer, antifungal, and antiviral properties. Both EGCG and EGC catechins are known for their immunomodulating and anti-inflammatory activities.[32]

Tumeric

Turmeric (*Curcuma longa* [syn. *Curcuma domestica*]) is a member of the ginger family. Research has shown that curcumin, the primary active constituent in turmeric, has numerous pharmacologic bioactivities, including antioxidant, antimicrobial, and anti-inflammatory properties. Studies indicate that curcumin is a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation. Both scientific and clinical trials have shown curcumin's potent inflammatory action.[33]

HEALTH-PROMOTING LIFESTYLE

Physical activity

Research has shown that individuals who expend more physical energy during the day experience a more restful night sleep. Walking is perhaps the easiest, most accessible, and effective means of being physically active. Movement exercises such as yoga and qigong expand flexibility while enhancing mind-body integration. Research evidence clearly indicates that regular physical activity, at least 30 minutes 3 times per week, is an important factor to guard against the negative effects of stress and helps alleviate anxiety, depression, and insomnia by increasing serotonin levels.

Restful sleep

The importance of proper rest and sleep for maintaining wellness and during times of stress and illness cannot be overemphasized. The immune system functions at its optimum levels when the parasympathetic nervous system assumes control of physiological functions, which occurs during periods of rest, relaxation, sleep, and meditation. It is during this time when potent immune compounds are released and immune functions are enhanced.[34,35] A healthy individual requires a minimum of 6 to 10 hours of sleep each night to feel energetic, alert, and vibrant.

Laughter

Research studies show that laughter reduces the level of stress hormones such as cortisol and adrenaline while it increases the levels of health and mood-enhancing hormones, endorphins, and neurotransmitters. Laughter has also been found to increase the immune system, which is often compromised during times of emotional and physical stress. These findings lend further support to the fact that laughter is like a spoonful of medicine.

Connecting with nature

Human beings evolved with nature, yet today most Americans spend 90% of their time indoors, separated from the majestic beauties of nature, natural sunlight,

and fresh air. Connecting to nature is uplifting, balancing, and inspirational to the mind, body, and spirit.

RELAXATION TECHNIQUES

The art of producing deep relaxation with any technique requires learning how to breathe. By focusing attention on the breath, it can alter the state of consciousness and induce relaxation. An easy-to-learn breathing technique involves inhaling while slowly counting to 4, pausing and holding the breath for a count of 7, and then slowly and completely exhaling at the count of 8. As the air flows out of the mouth, imagine all the tension and stress leaving the body. Then, repeat this process until a deep sense of relaxation is achieved.

Mindfulness mediation

Restful awareness is the state when the mind-body system integrates into a deep state of rest while the mind is awake. The most direct way to experience restful awareness is through meditation. During meditation, the breathing slows, blood pressure decreases, and stress hormones rapidly decline. Individuals who practice meditation on a daily basis develop less heart disease, hypertension, anxiety, and depression. Research has demonstrated that meditation offers a wide range of health improvements including its positive effects on mood disturbances, as in anxiety and depression.

Progressive muscle relaxation

This relaxation technique is based on the concept that the body responds to anxiety and stress-provoking thoughts and situations with muscle tension. This physiological response of muscle tightening, in turn, increases the subjective experience of anxiety and stress. Deep muscle relaxation techniques are known to help reduce physiological tension and as a result decrease the subjective experience of anxiety and stress.

Although muscle relaxation techniques vary, the underlying concept remains the same. First, begin by lying comfortably on the floor or in a chair, take a few deep slow breaths while focusing your attention on the different parts of your body, becoming aware of any muscle tension. Then, begin by curling your toes tightly, hold for a moment, and then slowly release, being conscious of the removal of tension in this area. Continue this process of "tensing and relaxing" the different muscle groups in your legs, arms, shoulders, and back, progress to your facial and scalp muscles, ending with your hands by clenching your fists, then slowly release, and feel the tingling sensation. Remain still for a few moments as you enjoy the release of tension throughout your body. This progressive muscle relaxation technique can easily be incorporated into a 10-minute daily routine, first in the morning and then again before going to sleep.

SPIRITUAL CONNECTION

The term *spirituality* may hold different meaning to different people. It may involve a daily meditation practice, a walk taken in nature, a gathering with a religious community to pray and worship, or simply an individual's prayer. Creating regular spiritual involvement honors our spiritual well-being by allowing us to connect more deeply with ourselves, with others, and with the Divine power that connects us to all. It provides comfort and a shelter during difficult, stressful times and in moments of despair.

REFERENCES

1. Snijder EJ, Bredenbeek PJ, Dobbe JC, et al. Unique and conserved features of genome and proteome of SARS-coronavirus, an early split-off from the coronavirus group 2 lineage. *J Mol Biol*. 2003;331(5):991-1004.
2. Zheng DP, Ando T, Fankhauser RL, Beard RS, Glass RI, Monroe SS. Norovirus classification and proposed strain nomenclature. *Virology*. 2006;346(2):312-323.
3. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. *Trends Microbiol*. 2016;24(6):490-502.
4. Peiris JS, Guan Y, Yuen KY. Severe acute respiratory syndrome. *Nat Med*. 2004;10(suppl 12):S88-S97.
5. Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology*. 2003;8(suppl):S9-S14.
6. Lee JY, Kim YJ, Chung EH, et al. The clinical and virological features of the first imported case causing MERS-CoV outbreak in South Korea, 2015. *BMC Infect Dis*. 2017;17(1):498.
7. Wang W, Lin XD, Guo WP, et al. Discovery, diversity and evolution of novel coronaviruses sampled from rodents in China. *Virology*. 2015;474:19-27.
8. Li W, Shi Z, Yu M, et al. Bats are natural reservoirs of SARS-like coronaviruses. *Science*. 2005;310(5748):676-679.
9. Lau SK, Woo PC, Li KS, et al. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. *Proc Natl Acad Sci U S A*. 2005;102(39):14040-14045.

10. Wang W, Lin XD, Liao Y, et al. Discovery of a highly divergent coronavirus in the Asian house shrew from China illuminates the origin of the alphacoronaviruses. *J Virol*. 2017;91(17):e00764-17.
11. Hamre D, Procknow JJ. A new virus isolated from the human respiratory tract. *Proc Soc Exp Biol Med.* 1966;121:190-193.
12. McIntosh K, Becker WB, Chanock RM. Growth in suckling-mouse brain of "IBV-like" viruses from patients with upper respiratory tract disease. *Proc Natl Acad. Sci U S A*. 1967;58(6):2268-2273.
13. Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020;579(7798):265-269.
14. Gorbalenya AE, Baker SC, Baric RS, et al. The species, severe acute respiratory syndrome- related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. A consensus statement: Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. *Nat Microbiol*. 2020;5:536-544.
15. World Health Organization. WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020. Accessed April 4, 2020.
16. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): how COVID-19 spreads. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html. Accessed April 4, 2020.
17. Bowie AG, Unterholzner L. Viral evasion and subversion of pattern-recognition receptor signalling. *Nat Rev Immunol*. 2008;8(12):911-922.
18. Williams AE. *The Innate Immune System. Immunology: Mucosal and Body Surface Defences*. Chichester, England: John Wiley & Sons Ltd; 2011:20-40.
19. Koenderman L, Buurman W, Daha MR. The innate immune response. *Immunol Lett*. 2014;162:95-102.
20. Tosi MF. Innate immune responses to infection. *J Allergy Clin Immunol*. 2005;116(2):241-249.
21. Beutler B. Innate immunity: an overview. *Mol Immunol*. 2004;40(12):845-859.
22. Horner SM. Activation and evasion of antiviral innate immunity by hepatitis C virus. *J Mol Biol*. 2014;426:1198-1209.
23. Dinarello CA. Immunological and inflammatory functions of the interleukin-1 family. *Annu Rev Immunol*. 2009;27:519-550.
24. Dolinay T, Kim YS, Howrylak J, Hunninghake GM, An CH, Fredenburgh L. Inflammasome-regulated cytokines are critical mediators of acute lung injury. *Am J Respir Crit Care Med*. 2012;185(11):1225-1234.
25. Chen IY, Ichinohe T. Response of host inflammasomes to viral infection. *Trends Microbiol*. 2015;23(1):55-63.
26. National Institute of Allergy and Infectious Disease. Coronaviruses; information for researchers. https://www.niaid.nih.gov/diseases-conditions/coronaviruses. Accessed April 4, 2020.
27. National Center for Complementary and Integrative Health. In the news: coronaviruses and "alternative" treatments. https://www.nccih.nih.gov/health/in-the-news-coronavirus-and-alternative-treatments. Accessed April 4, 2020.
28. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): how to protect yourself and others. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html. Accessed April 4, 2020.
29. Oldways Cultural Food Traditions. The Mediterranean diet. https://oldwayspt.org/traditional-diets/mediterranean-diet. Accessed April 16, 2020.
30. Ross SM. Generalized anxiety disorder (GAD); efficacy of standardized *Matricaria recutita* (German chamomile) extract in the treatment of generalized anxiety disorder. *Holist Nurs Pract*. 2013;27(6):366-368.
31. Barak V, Halperin T, Kalick I. The effect of sambucol, a black elderberry-based, natural product, on the production of human cytokines: I inflammatory cytokines. *Eur Cytokine Netw*. 2001;12(2):290-296.
32. Li J, Dongfeng S, Shengnan W, Yadong D, Jiyong Z, Jinyan G. Antiviral effect of epigallocatechin gallate via impairing porcine circovirus type 2 attachment to host cell receptor. *Viruses*. 2020;12(2):E176.
33. Ross SM. Turmeric (*Curcuma longa*): effects of curcuma longa extracts compared\with ibuprofen for reduction of pain and functional improvement in patients with knee osteoarthritis. *Holist Nurs Pract*. 2016;30(3):183-186.
34. Prather AA, Deverts-Janicki D, Martica HH, Cohen S. Behaviorally assessed sleep and susceptibility to the common cold. *Sleep*. 2015;38(9):1353-1359.
35. Ross, SM. Insomnia: an integrative approach to stress-induced insomnia. *Holist Nurs Pract*. 2011;25(5):266-269.