Lifestyle Medicine and the Microbiome: Holistic Prevention and Treatment

Shawn Manske, ND

Shawn Manske, ND, Assistant Director of Clinical Education, Biocidin Botanicals, Watsonville CA, USA.

Corresponding author: Shawn Manske, ND
E-mail: drmanske@biocidin.com

Chronic diseases are the leading causes of illness, mortality, and healthcare costs worldwide.[1,2] Yet many chronic diseases are the result of unhealthy lifestyles and environmental factors, and physicians can successfully prevent and treat them through the application of lifestyle medicine (LM). According to the American College of Lifestyle Medicine (ACLM), LM is a medical approach that focuses on using healthy lifestyle changes as the primary way to prevent and treat chronic conditions such as heart disease, type 2 diabetes, and obesity.[3]

Lifestyle Medicine

Doctors who practice LM receive training to use evidence-based, holistic lifestyle changes to try and prevent, treat, and sometimes reverse chronic illnesses. A practitioner-led focus on helping patients adopt healthier lifestyle habits and alter environmental factors within their control can vastly improve patients' health while minimizing economic hardship due to chronic illness. This requires education, training, and communication about LM for healthcare professionals and patients, as well as a positive approach to helping patients implement healthy changes.

LM rests on six pillars to promote and maintain health[4]: (1) a whole-food, plant-predominant eating pattern, (2) physical activity, (3) restorative sleep, (4) stress management, (5) avoidance of risky substances, and (6) positive social connections.

Physicians founded the ACLM in 2004, and it's a 501c3 nonprofit organization.[2] Although LM may seem like a modern medical specialty, its principles have existed for centuries. Hippocrates, the ancient Greek philosopher and physician considered to be the father of medicine, advised that to stay healthy, one should "avoid too much food, too little toil.[4]" He urged physicians to consider not only the disease itself but also factors such as diet, exercise, sleep, and alcohol consumption. The principles and practices of naturopathic medicine, which was founded in the USA in 1901, also include the core pillars of LM.[4]

LM focuses on introducing daily, healthy habits to improve physiological function and optimize wellness. It draws on various disciplines, including nutrition science, health and wellness coaching, exercise physiology, sleep science, behavioral change, psychology, and addiction medicine.[4] Unlike conventional medicine, which often relies on medications to treat specific conditions, LM emphasizes overall wellness and prevention through sustained healthy practices that offer broad health benefits.

One of the ACLM's key objectives is ensuring that prescribed treatments are evidence-based, relying on epidemiological studies and randomized, controlled trials that demonstrate the reversal of many prevalent and costly chronic diseases.[4] Over the past few decades, extensive research has examined the health benefits of exercise, diet and nutrition, maintenance of a healthy weight and body composition, and smoking avoidance. For example, a landmark study in the *Journal of the American Medical Association (JAMA)* in 1993 estimated that approximately 80% of premature deaths in the USA were due to poor lifestyle choices.[4] Publications, such as the Diabetes Prevention Program, the Lifestyle Heart Trial, the PREDIMED Study, the Lyon Heart Study, and the Framingham Heart Study, have established LM as a leading paradigm in modern-day medicine.[4]

In Westernized countries, three major conditions that primarily result from poor lifestyle choices have contributed to or caused morbidity and mortality: inflammation, obesity, and insulin resistance.[3] An unhealthy diet, sedentary lifestyle, high stress, emotional conflict, and prescription medications can all contribute to microbial dysbiosis—an imbalance of the microbial communities in our bodies, oxidative stress, and cellular injury. These mechanisms can then activate chronic inflammatory pathways that play a significant role in the development of chronic diseases such as obesity, type 2 diabetes, cardiovascular disease, cancer, and mental health disorders such as depression and anxiety.

Microbial dysbiosis, and by extension, the microbiome, have evolved as a significant area of research due to their extensive influence on human physiology. While the six pillars of LM don't consider the microbiome directly, it's a modifiable factor intimately linked to these pillars that an LM approach can incorporate.

The Microbiome

According to Malard et al, a microbiota is defined as an "assemblage of microorganisms—all the bacteria, archaea, eukaryotes, and viruses—present in a defined environment.[5]" It's found in all multicellular organisms, including plants. The similar term microbiome describes either the collective genomes of the microorganisms that reside in an environmental niche or the microorganisms themselves.[5] Manos indicates that microbiomes exist in several areas of the human body, including the oral cavity, skin surface, intestinal tract, esophagus, and lungs.[6] However, the microbiome of the gastrointestinal tract is the most studied.

In both host and environmental settings, bacteria typically thrive in communities called biofilms. This preference for communal living and their exceptional communication ability gives them an advantage within a microbiome. Bacteria use small molecules known as autoinducers to communicate as they form these communities. Through intraspecies communication, known as quorum sensing (QS), they can gauge their population size and detect and interact with other bacterial species. This cooperative interaction enables multiple species to work together, contributing to the community and creating a cohesive microbiome.[7]

Most human microbiome research uses noninvasive fecal samples as proxies for the microbiota and focuses on the microbial community within the large intestine.[7] This portion of the gastrointestinal (GI) tract harbors the greatest microbial biomass of any organ or surface of the human body.[8] According to Walter and Ley, each milliliter of the large intestine holds approximately 10^{11} microbial cells compared to 10^{8} cells in the small intestine.[8]

Research suggests an estimated 150 to 400 species reside in a person's gut, with most species belonging to the Bacteroidetes, Firmicutes, Actinobacteria, and Proteobacteria phyla.[9] Beyond the data for individuals, data collected by the Human Microbiome Project and the metagenomic analysis database MetaHIT reveal approximately 3000 bacterial species isolated from human feces.[7] The composition of these taxa differs greatly from one person to another and can change significantly within the same person throughout his or her lifetime.[8]

Early colonization and development of the human microbiome begin at birth, and various factors influence it, including the mode of delivery, diet, environment, and antibiotic exposure.[10] During vaginal birth, babies are exposed to their mother's vaginal and gut microbiota, which is dominated by Lactobacillus, Prevotella, and Sneathia spp. By contrast, cesarean section deliveries result in initial colonization by skin and environmental microbes and is dominated by Staphylococcus, Corynebacterium, and Propionibacterium spp.[11] Interestingly, some research has challenged the long-held belief that the prenatal gut is sterile, such as Perez-Munoz et al's study that suggested that some small-scale colonization may occur in utero, although this claim remains controversial.[12]

Breastfeeding also influences the infant microbiome by providing beneficial bacteria and oligosaccharides that promote the growth of specific microbial communities.[13] With the introduction of solid foods, an infant's microbiome begins diversifying and stabilizing, more closely resembling that of an adult at around three years of age.[14] Early microbiome colonization is necessary to support the development of the immune and digestive systems and protection against pathogens.

Disruptions in this process early in life, such as through antibiotics' use or the absence of breastfeeding, can have lasting health effects, including increased risk for inflammatory disorders, autoimmune diseases, neurological disorders, and obesity.[15]

Antibiotic exposure in early life can trigger intestinal dysbiosis by disrupting the commensal and pathogenic bacteria. Perez-Munoz et al found that the impacts will depend upon the age, duration, dosage, and frequency at the time of treatment.[12] Those researchers noted a reduction in diversity by more than 25% with broad-spectrum antibiotic use, with this reduction including a decrease in the abundance of Bifidobacterium, the predominant colonizer of the neonatal gut, and an increase in the ratio of Firmicutes/Bacteroidetes with early-life exposure.

Perez-Munoz et al also found that while these effects appear to be short-term and recover once treatment ends, concern exists for long-term health impacts, with the potential to produce antibiotic-resistant genes in the gut. Those researchers also found that these genes may elevate inflammatory cytokines, impact insulin sensitivity, and affect short-chain fatty acid (SCFA) metabolism and production of bile acids.

While much of the research on the human microbiome focuses on the gastrointestinal (GI) tract, each body part has a distinct microbial-community composition. The bacterial 16S rRNA data reveal a clustering of certain microbial taxa in particular body sites, such as the surface of the skin, gut, oral cavity, airways, or urogenital tract, regardless of the host's gender, age, weight, or any other host metric.[15]

Researchers have sought to define a set of core microbiota in human intestinal tracts with comparisons of fecal 16S rRNA testing. For example, Ruan et al revealed that a significant abundance of bacterial phylotypes are continuously present and thus comprise a stable microbial core that includes Bacteroides, Eubacterium, Faecalibacterium, Alistipes, Ruminococcus, Clostridium, Roseburia, and Blautia.[16] Within these phylotypes, Faecalibacterium prausnitzii, Oscillospira guillermondii, and Ruminococcus obeum are the top three taxa that all adults share.[17]

The human body provides a variety of environmental niches, nutrients, and metabolites for microbes—essentially symbiotic organisms—to grow and thrive in. At the same time, the microbiota plays a crucial role in various bodily functions, including metabolism, immune stimulation, barrier maintenance, and signaling to almost every organ.[6]

Role of Microbiome

Digestive System

The microbiota of the GI tract plays a significant role in supporting digestion and the assimilation of nutrients. Certain bacterial strains and archaea, such as Methanobrevibacter, aid in the breakdown of dietary components that humans can't metabolize, generating essential nutrients, vitamins, and various metabolites that support physiological functions.[17]

Microbial metabolites, such as short-chain fatty acids (SCFAs) and bile acids, can act as signaling molecules that modulate hormone secretion and energy homeostasis. The gut microbiota's fermentation of nonhost-digestible dietary fibers generate SCFAs, with more than 95% of SCFAs derived from gut microbes being made up of acetate, propionate, and butyrate.[18] SCFAs help regulate gut-microbiota composition, gut-barrier integrity, appetite, energy homeostasis, gut hormone production, circadian clocks, inhibition of proinflammatory cytokines, stimulation of water and sodium absorption, and the modulation of systemic immune responses.[19] Furthermore, gut microbes produce and metabolize hormones and neuropeptides such as ghrelin and leptin, which are involved in appetite and metabolic regulation.[20]

Immune System

The microbiota interacts directly with the cells of both the innate and adaptive, intestinal immune system to maintain intestinal balance.[6] This partnership is vital for health and mutually beneficial, allowing the immune system to tolerate beneficial microbes while still being capable of mounting an inflammatory response against harmful pathogens. Disturbances in the gut microbiota may enable the growth of pathogenic bacteria; damage the intestinal barrier, leading to increased exposure to microbes and toxins; prime the immune system for an excessive inflammatory response; and reduce the production of beneficial microbial products such as SCFAs.[6] This may lead to immune imbalance, heightening the risk for immune and inflammatory disorders.[6]

Nervous System and Mental Health

The gut-brain axis (GBA) connects the network of nerves in the GI tract, known as the enteric nervous system, and the central nervous system (CNS) through multiple communication pathways, including the autonomic, neuroendocrine, enteric, and immune-system pathways.[21] It's bidirectional, meaning the microbiome and GI tract influence the brain, and the brain, in turn, influences the GI tract.[22]

These pathways combine through the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis to create the GBA, allowing the gut to influence mood, cognition, and mental health while the brain influences intestinal activities, such as motility, immune activity, and serotonin metabolism.[22] Disruption of neural pathways in the gut-brain axis has been implicated in the pathogenesis of various GI and neurological disorders, including irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), and mood disorders.[23] Additionally, Chen et al have implicated alterations in neurotransmitter signaling, neuroinflammation, and stress-response pathways in the GBA in the pathophysiology of anxiety and depression as well as Alzheimer's disease (AD), dementia, Parkinson's disease (PD), Autistic Spectrum Disorder (ASD), and schizophrenia, highlighting the interconnectedness of gut health and mental well-being.[24]

The microbiome's impacts on other bodily systems and functions are copious and broad-ranging. Mounting evidence, such as that from Hou et al's study, has confirmed that disruptions to the microbiota are associated with the development of cardiovascular diseases, cancer, respiratory diseases, diabetes, IBD, brain disorders, chronic kidney diseases, and liver diseases.[25]

Lifestyle Factors and the Microbiome

Numerous lifestyle factors influence the human microbiome, significantly impacting its composition and function. These factors include diet, exercise, stress, sleep, and antibiotic use.

Diet is one of the most influential factors shaping the microbial communities in the gut, and the interplay between diet, the gut microbiome, and the host's health is complex. Changes in dietary patterns can directly influence the composition and functionality of the gut microbiota through the availability of macro- and micronutrients in the gut.[26]

A diet rich in fiber, fruits, vegetables, fermented foods, unsaturated fatty acids, and polyphenols promotes a diverse and healthy microbiome.[27] Conversely, diets high in processed foods, sugars, and fats can lead to dysbiosis, an imbalance in the microbial community.[28] In Westernized countries, the typical diet includes many calorically dense, ultra-processed foods that are low in fiber and high in saturated fats, salt, and refined carbohydrates. Such a diet may result in harmful health consequences, such as obesity, metabolic syndrome, and cardiovascular disease.[28]

Researchers have found that exercise and regular physical activity can positively influence the microbiome's diversity and composition. For example, Clarke et al found that exercise can enhance microbial diversity, promote the growth of beneficial bacteria, and improve gut health.[29] Hughes and Holscher's study suggested that gut microbes support the effects of diet and nutrition on athletic performance by influencing microbial metabolite production, gastrointestinal physiology, and immune modulation.[30]

Stress can be defined as physical, psychological, or environmental. To varying extents, it is a constant part of modern daily life.[27] Activation of the human stress-response system, the HPA axis, caused by severe, chronic, or uncontrolled stressors, is associated with adverse physical and mental health outcomes.

Chronic stress can negatively impact the microbiome by altering its composition and function. Perler et al have linked stress to gut dysbiosis, suggesting that the intestinal microbiota could act as drivers of chronic-stress responses.[27] Galley et al have linked stress-induced changes in the gut microbiota to gastrointestinal issues, inflammation, and alterations in the gut-brain axis.[31]

Sleep is a vitally important facet of health and wellness, and sleep deficiency may contribute to adverse health conditions. Insufficient sleep affects circadian hormonal profiles and inflammatory markers, impairs HPA-axis function and may modulate attention, executive functioning, and decision-making.[32] Interestingly, Han et al's study suggests that abnormal sleep patterns and insufficient duration can affect the gut microbiota's composition, diversity, and function through the GBA, a bidirectional communication network between the microbial communities in the GI tract and the CNS.[33] Furthermore, Han et al's study, The interplay between sleep and gut microbiota, asserts that the microbiome is essential for the maintenance of normal sleep physiology.[33]

These lifestyle factors collectively shape the microbiome, influencing overall health and disease risk. By understanding their impact, practitioners can implement strategies to maintain a healthy microbiome and prevent related health issues.

LM and the Microbiome

Lifestyle medicine, which emphasizes the use of evidence-based lifestyle interventions to prevent, treat, and reverse chronic diseases, significantly influences the microbiome and thereby improves overall health. Its components include a balanced diet, regular physical activity, adequate sleep, stress management, and mindful use of antibiotics and other drugs. A diet rich in whole foods, fiber, and fermented products fosters a diverse and resilient microbiome, which is essential for optimal digestion, immune function, and metabolic health.

Regular exercise enhances microbial diversity and supports beneficial bacterial populations, while stress-reduction techniques such as mindfulness and meditation mitigate the adverse effects of chronic stress on the gut microbiota. Adequate sleep promotes a stable and healthy microbial community, reducing the risk of metabolic and inflammatory disorders. Careful use of antibiotics, in addition to probiotics—beneficial, commensal microorganisms—and prebiotics—fibers that support the growth and diversity of probiotics—can help maintain microbial balance, preventing dysbiosis and associated health problems. By incorporating these lifestyle interventions, LM supports a healthy microbiome and contributes to overall well-being and the prevention of chronic diseases.

LM practitioners should take care to educate their patients about the microbiome, including how their choices and behaviors may negatively impact it and how that impact may contribute to their health concerns and risks. By providing a thorough microbiome assessment that includes stool-based microbial testing, practitioners can offer a personalized LM approach, modifying microbial balance positively and improving overall health.

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