A Clinician's Primer on the Role of the Microbiome in Human Health and Disease

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CME Activity

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The authors report no competing interests. The authors discuss the role of prebiotics, probiotics, synbiotics, and fecal microbiota transplantation as potential microbiota restorative therapies and note that these are investigational and not approved by the US Food and Drug Administration.

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Abstract

The importance of the commensal microbiota that colonizes the skin, gut, and mucosal surfaces of the human body is being increasingly recognized through a rapidly expanding body of science studying the human microbiome. Although, at first glance, these discoveries may seem esoteric, the clinical implications of the microbiome in human health and disease are becoming clear. As such, it will soon be important for practicing clinicians to have an understanding of the basic concepts of the human microbiome and its relation to human health and disease. In this Concise Review, we provide a brief introduction to clinicians of the concepts underlying this burgeoning scientific field and briefly explore specific disease states for which the potential role of the human microbiome is becoming increasingly evident, including *Clostridium difficile* infection, inflammatory bowel disease, colonization with multidrug-resistant organisms, obesity, allergic diseases, autoimmune diseases, and neuropsychiatric illnesses, and we also discuss current and future roles of microbiome restorative therapies.

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New scientific literature regarding the human microbiome has recently increased, with more than 90% of the nearly 4000 articles indexed by PubMed on the topic being published within the past 5 years. Although the clinical relevance of this field may initially seem esoteric to the practicing clinician, there is growing realization of the role our commensal microbiota plays in human health and disease. It is likely that in a short time, understanding the basic concepts about the interactions between humans and their microbiome will be as important to clinicians as understanding concepts of genetics or germ theory. This article provides a brief introduction to clinicians of the concepts underlying this

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burgeoning scientific field and briefly explores specific disease states for which the potential role of the human microbiome is becoming increasingly evident.

The term *microbiome* refers to the total number of microorganisms and their genetic material and is contrasted from the term *microbiota*, which is the microbial population present in different ecosystems in the body. The average human has 100 trillion microbes in the gut, which is 10 times more than the cells in the human body; hence, the commensal bacteria and fungi that inhabit our bodies vastly outnumber our human cells. The number and variety of bacteria exponentially increase from the proximal to the distal gastrointestinal tract, with the colon harboring most of the gut microbiota. Although it had been largely thought that these microbes are merely tenants on our skin, gut, and mucosal surfaces, it has become increasingly evident that our microbiome is crucial to our health and well-being.[1] The human microbiome has coevolved with humans throughout the millennia, with the development of specific communities of microbes occupying specific anatomical niches within the human body.[2] Human microbial ecology and macroscopic ecology have many parallels that help with the conceptual understanding of the microbiome. Just as one can expect certain kinds of plants and animals on different tropical beaches, one can expect similar microbial ecologic systems in specific anatomical areas that will be common among different people because they are similar, although specific, microecosystems (eg, predominance of Bacteroidetes and Firmicutes in the colon and Firmicutes and Proteobacteria in the mouth).[3,4] The specific balance of microbial diversity within specific anatomical locations will differ among people because of variations, such as in hygiene, social behaviors, and genetics.[5,6] The gut microbiota may differ at different time points at the same anatomical location within the same person owing to environmental changes.[7] Diet plays a major role in defining the composition of the gut microbiota. In addition, metabolites produced by gut bacteria enter the bloodstream by absorption and enterohepatic circulation. Commensal microbiota produces metabolites that may have a positive effect on the host, including anti-inflammatory and antioxidant activity, regulation of gut barrier function, and production of vitamins and energy sources.[1]

Colonization with normal commensal organisms begins shortly after birth on exposure to vaginal microbiota. Infants continue to be introduced to new flora through routine activities with other humans, including feeding and play, resulting in the establishment of the microbiome on the skin, gut, and mucosal surfaces. Introduction and reintroduction of flora continues throughout life from our routine interactions with each other. The establishment of the gut microbiota starts at birth, reaches its maximum diversity at adolescence, and remains stable until the later stages of life, where the microbiota becomes comparatively less diverse with reduced stability, thus predisposing elderly individuals to conditions associated with decreased diversity, such as *Clostridium difficile* infection (CDI).[8] The 4 predominant bacterial phyla in the gut are Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria, followed by archaea, viruses, and fungi.

Rather than simply occupying space on our bodies, our microbiome is essential to several aspects of normal development through interactions with the mucosal immune system. The interaction of our flora with our immune system results in several processes, such as the secretion of secretory IgA and the release of endogenous antimicrobial peptides, among others, that help maintain normal homeostasis of the microbiome.[9] These interactions are also vital to the maturation and maintenance of the mucosal immune system, abnormalities of which have been linked to diseases of anergy and autoimmunity.[9,10] Several aspects of life in modern society, such as antimicrobials, sanitation, vaccination, and dietary changes, have profound and lasting effects on our microbiome. Alterations and imbalance of the gut microbiome have been implicated in gastrointestinal illnesses such as CDI, antibiotic-associated diarrhea, irritable bowel syndrome (IBS), and pathogen colonization (such as vancomycin-resistant enterococcus), and systemic conditions, such as autoimmune and allergic diseases, metabolic derangements (eg, obesity), and neuropsychiatric conditions (eg, autism).[5,7,11-16] Most of the studies that provide information regarding the role of the gut microbiota in disease report alterations of specific community structures in individuals with disease compared with healthy