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Clinical care is evolving: The microbiome for advanced practice nurses

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Abstract

Over the course of four billion years, humans have developed an intimate relationship with the more than 37 trillion microbes that inhabit our bodies. This relationship runs the gamut from symbiosis to pathogenesis. The number of microbial cells is roughly equivalent to that of mammalian cells in the body. However, due to substantial microbial diversity in host-associated communities, the genetic content of the microbiome is roughly 150 times greater than that of the human genome. Microbial genes encode for proteins capable of producing a wide variety of molecules essential for our health and survival. Many factors such as mode of birth, diet, chlorination of water, and medications significantly affect the richness and diversity of the microbiome. Advanced practice nurses have important roles to play as clinicians, scientists, educators, and patient advocates as our understanding of the microbiome's effects on health becomes better articulated. An understanding of how the microbiome can affect an individual's health or the efficacy of treatment will soon be essential in the clinical setting, and nurses should be encouraged to educate themselves on the relationship between our microbial partners, the environment, and human health.

Keywords

Advanced practice nursing; genomics; microbiota; noncommunicable disease; nurse practitioners

The tree of life consists of three branches or domains: bacteria, archaea, and eukaryota. Prokaryotes (bacteria and archaea) are single-celled organisms that lack a nucleus and are thought to have split from a common ancestor approximately 3.5 billion years ago (Blaser, 2014). Archaea share a more recent common ancestor with eukaryotes (animals, plants, fungi), and they also share some biological features with eukaryotes despite being single cells. A distinguishing feature of eukaryotes is the presence of a membrane-bound nucleus

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used in part to protect the cell's genetic information. Eukaryotic cells and prokaryotic cells have coexisted intimately in the natural environment over billions of years.

In addition to colonization of natural environments (e.g., soil and water), microorganisms grow intimately in association with complex life forms, such as animals and plants. Here, the relationship between microorganism and host organism runs the gamut from symbiosis to pathogenesis, and long-term interactions lead to co-evolution of host and microbe. Mammalian hosts provide substrate for microbial growth (both colonization surfaces and nutrients), and these are exploited by microbial communities. Given our common ancestry and our proximity to the microbial world over the course of our evolution, it should come as no surprise that humans and microbes have developed a unique symbiotic relationship over time. The human microbiome, for example, consists of approximately 37 trillion microbial cells, and collectively, these microbial cells have the same biomass as the human brain, weighing about three pounds (Sender, Fuchs, & Milo, 2016). The number of microbial cells is roughly equivalent to that of mammalian cells in the body; however, due to substantial microbial diversity in host-associated communities, the genetic content of the microbiome is roughly 150 times greater than that of the human genome (Human Microbiome Project Consortium, 2012). Microbes can be found in or on every bodily surface, although the majority of host-associated microbiota reside in the gut. Microbial genes encode for proteins capable of producing a wide variety of molecules essential for our health and survival, including molecules responsible for the development of the innate and adaptive immune systems, synthesis of vitamins (B, B12, thiamine and riboflavin, and vitamin K), production of neurotransmitters, and synthesis of short chain fatty acids to maintain integrity of the intestinal barrier (Ursell, Metcalf, Parfrey, & Knight, 2012). Recent studies have observed interactions between the gut microbiome and mammalian genome that appear to play a role in regulating gene expression by altering host DNA methylation, histone modification, and noncoding RNAs (Qin & Wade, 2018).

We first acquire our microbiomes during pregnancy and the birthing process. Babies who are born vaginally have a microbiome that resembles their mother's birth canal, vagina, oral cavity, and skin. Microbes acquired during the journey through the birth canal may confer protection against disease across the life span (Levin et al., 2016). Microbial communities acquired from around the nipple and in the mother's breast milk during breast-feeding also contribute to our microbiome shortly after birth. For those born via caesarian section, bypassing the birth canal, the microbiome resembles the microbiome of the mother's and other caregiver's oral cavity and skin (Levin et al., 2016). Evidence has emerged suggesting that babies born via caesarian section may be more prone to developing childhood allergies and noncommunicable diseases, like asthma and obesity, into adulthood (Neu & Rushing, 2011). This has led to an experimental practice called "seeding" the microbiome. The seeding process involves inoculating a cotton gauze with secretions from the vagina during the birthing process. The inoculated gauze is used to transfer the vaginal flora to the eyes, mouth, nose, and skin of the newborn after caesarian section delivery. A recent study found that microbiome seeding was successful in partially restoring the microbiome after caesarian delivery; however, a risk of the procedure is the potential transfer of pathogens from mother to infant (Dominguez-Bello et al., 2016). Thus, improved screening for potential pathogens,

including those causing sexually transmitted diseases, before the procedure will be necessary.

Our microbial partners also play an important role in how we metabolize certain drugs. A recent study of 76 human gut bacterial isolates led by Andrew Goodman of the Yale University School of Medicine linked variations in interpersonal drug metabolism of 271 commonly used, orally administered, drugs to interpersonal variability in the microbial genetic content and metabolic activity (Zimmermann, Zimmermann-Kogadeeva, Wegmann, & Goodman, 2019). The authors reported that enzymes produced by microbiota in the gut metabolized 176 of the 271 drugs studied (64.9%). Variations in microbiota-encoded enzymes can contribute to variation among individual's response to drugs, the efficacy of treatment, and many adverse drug reactions (Zimmermann et al., 2019). Commonly used drugs most likely to affect the taxonomic structure and metabolic function of the gut microbiome include proton pump inhibitors, metformin, antibiotics, and laxatives (Vila et al., 2019). As our knowledge of the microbiome progresses, it is increasingly clear that consideration of the bidirectional effects of the microbiome on drug metabolism will be important for pharmaceutical companies during drug development, for advanced practice nurses when prescribing treatment, and for nurses at the point of care who administer drugs and assess drug-related adverse events.

The most successful clinical application of the microbiome to date has been the use of fecal microbiota transplantation (FMT) (van Nood et al., 2013). Fecal microbiota transplantation treatments involve transferring "healthy" fecal material from a donor to a person experiencing disease via a colonoscopy or in pill form (Kao et al., 2017). The most common use of FMT is to treat refractory *Clostridium difficile* infections; however, other treatments include obesity, Parkinson disease, irritable bowel syndrome, fibromyalgia, multiple sclerosis, metabolic syndrome, and autism (Choi & Cho, 2016) with varying rates of success. The success rate for remission of treatment-resistant *C. difficile* infections is consistently reported as 90% or higher (Kao et al., 2017). Fecal microbiota transplantation has become the standard treatment for *C. difficile* infections unresponsive to treatment in many centers in United States. However, FMT is not approved for any use by the US Food and Drug Administration (FDA) and should be considered an experimental treatment (FDA). Despite the overwhelming success of FMT in treatment-resistant *C. difficile*, posttransplant adverse events have been reported. Case studies reported that unexpected and persistent weight gain after stool was transferred from an obese donor to a lean recipient (Alang & Kelly, 2015). These effects had been observed previously in laboratory studies (Ridaura et al., 2013). In an exquisite study, Ridaura et al (2013) transplanted fecal microbiota from adult female twins discordant for obesity into germ-free mice and found that the transplanted microbiome modulated adiposity and metabolic phenotypes in the mice (Ridaura et al., 2013). Potential adverse effects of FMT are not limited to weight gain. In 2019, the FDA released a safety warning about the potential for serious or life-threatening infections related to the transfer of multidrug-resistant organisms (MDROs) after two immunocompromised adults developed invasive bacterial infections after FMT (U.S. Food and Drug Administration, 2019). One of the patients died. The FDA plays a role in monitoring the safety of the intervention and has issued several protections for patients receiving FMT, including screening donors for MDROs.

Multiple environmental factors contribute to maintenance of a healthy microbiome (Maki et al., 2019). There are several suggestions Advance Practice Nurses (APNs) can recommend to their patients to improve their microbiome health, and many relate to eating foods that enrich for healthy gut microbiota (prebiotics) and those containing microorganisms contributing to a healthy gut microbiome (probiotics). Over-the-counter probiotics are not regulated by the FDA, and contents may vary significantly from what is stated on the packaging. The best source of pre/probiotics is in whole foods, particularly fermented foods like kimchi, yogurt, kefir, and sauerkraut. The western diet high in animal fats (which may contain antibiotics) and sugar/fructose, and low in fiber has been proven to promote obesity and unhealthy microbial communities (dysbiosis) in the orogastrointestinal tract (Blaser, 2014). APNs can recommend a high-fiber diet derived from many different plant-based sources, as is found in the Mediterranean diet, as this promotes greater diversity and richness of microbiota communities. In addition, chemicals in municipal drinking water, such as chlorine, are also detrimental to the microbiome diversity, and thus, filtered water should be used when possible (Maritno, 2019). It is important that APNs should prescribe antibiotics when only when necessary. Overuse of prescribed antibiotics and antibiotics in our food system contribute to the rise of unhealthy microbiome phenotypes that contribute to noncommunicable disease. Jack Blaser, author of the *Missing Microbes*, makes a compelling case arguing that the overuse of antibiotics may be the root cause for many of the noncommunicable disease we see today reaching epidemic proportions including obesity, diabetes, and asthma (Blaser, 2014). Finally, do not be afraid to get dirty. Patients should be encouraged to work in the garden and spend time outdoors with the notable exception of immunocompromised patients. Microbes in the environment help us maintain a diverse microbiome, and oversanitation can kill beneficial bacteria along with the harmful bugs. Common sense dictates that this does not absolve nurses or other clinicians from frequent hand washing in an effort to prevent the spread of infectious diseases in the clinical setting.

Advanced practice nurses have important roles to play as clinicians, scientists, educators, and patient advocates, as our understanding of the microbiome's effects on health become more well articulated. Understanding the associations between the microbiome and an individual's health or the efficacy of treatment will be critical, particularly as these considerations become standard care in the clinical setting. Thus, nurses should be encouraged to educate themselves on the relationship between our microbial partners, the environment, and human health.

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