Health and the Human Microbiome: A Primer for Nurses

What findings about the GI and vaginal microbiota mean for patient care.

ABSTRACT: The profound impact of the human microbiome on health makes it imperative that nurses understand the basic structures and functions of the various microbial communities. In studying the human microbiome, advances in DNA and RNA sequencing technology offer benefits over traditional culture-based methods. Such technology has permitted more thorough investigations of microbial communities, particularly those of the gastrointestinal (GI) and female reproductive tracts. Although individual variations exist, each site exhibits distinct compositions. The diverse GI microbiota aid in digestion, mood regulation, and vitamin synthesis. While many factors affect the composition and functions of the GI microbiota, diet likely exerts the strongest influence. Vaginal microbiota tend to be less diverse, and mainly serve to protect women from infection. The composition of the vaginal microbiota is influenced by sexual activity, hygienic practices, medications, smoking, and other factors. Our increasing knowledge about the structures and functions of the GI and vaginal microbiota allows nurses to provide targeted, evidence-based education and care for various populations.

Keywords: dysbiosis, gastrointestinal microbiota, microbiome, vaginal microbiota

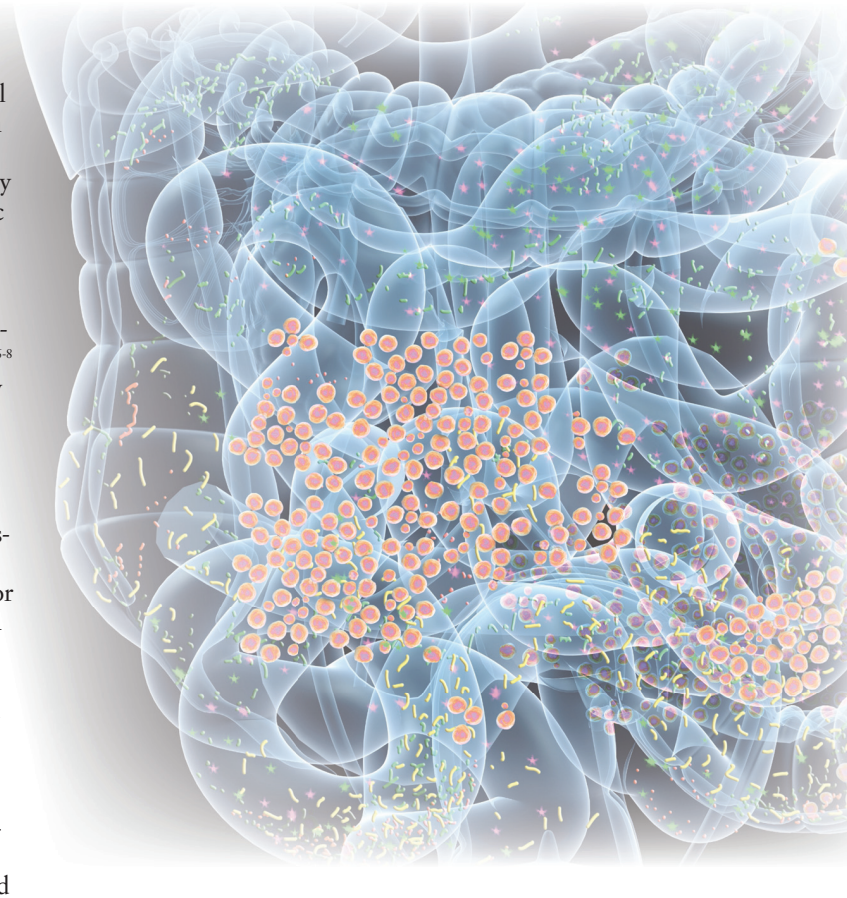
We are not alone. From the moment of birth, we travel through life with a diverse collection of microbes (called the human microbiome) living in and on our bodies. This microbiome has been studied for centuries, and over time, our understanding of the symbiotic relationship between microbes and humans has grown. It's now recognized that microbes, once unequivocally regarded as dangerous invaders, often serve us as integral companions, providing critical functions in fundamental human processes.

The human microbiome is so intrinsically linked to human physiology that it's now considered a discrete body organ in its own right.[1,2] Indeed, it's been estimated that the human body contains at least as many microbial cells as human cells, with microbial genes vastly outnumbering human genes.[3-5] Furthermore, the microbial communities that make up the human microbiome are found in every niche of the body, including on the skin, in the ears, and in the gastrointestinal (GI) and reproductive tracts. The impact that these various microbial communities have on human health makes it imperative for nurses to understand their basic structures and functions.

This article provides an overview of the current state of knowledge about the human microbiome and the implications for nursing practice. We focus particularly on the microbiota in the GI tract and the vagina, as these are the most commonly studied body sites.

STUDYING THE HUMAN MICROBIOME

Before DNA technology became readily available in the 1980s, researchers had limited options for studying the human microbiome. Microbes—mainly



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bacteria—were isolated from specimens such as stool samples or oral swabs and were typically grown in a laboratory under strictly specified conditions using culture-based techniques. Researchers then visually identified the cultivated species by their morphologic and phenotypic characteristics, such as shape, size, and reaction to biochemical staining. But the lack of differentiating features among single-celled microorganisms made the classification of cultivated species difficult, and the results were often inaccurate.[6-8] Culture-based techniques also precluded the ability to study in vivo microbial communities, because the conditions for the laboratory cultivation of most species were either unknown or restrictive.[6,7] Thus only a small fraction of the species that make up the human microbiome—those that could be grown easily under known conditions—were identified.

In the mid-1970s, Sanger developed a method for sequencing DNA, and in the ensuing decades DNA and RNA sequencing technologies have advanced. Such advances have permitted the development of molecular-based classification methods that rely on DNA and RNA sequencing rather than on laboratory cultivation and morphologic and phenotypic observations. Recent innovations have made possible large-scale and more cost-effective studies of microbial communities.[9,10]

The most common molecular-based technique used to study the human microbiome is 16S ribosomal RNA (rRNA) gene profiling. This technique can yield a highly detailed view of the entire bacterial community living in a site from which a specimen is taken. It's particularly useful with bacterial species that may be resistant to culture or are present in very small numbers.[6,7] Because the 16S rRNA gene is found in all species of bacteria, researchers use the technique to isolate bacterial DNA from a given specimen and to exclude human, viral, and fungal DNA that may also be present. The 16S rRNA gene also varies enough among bacterial species such that it permits precise species identification. Researchers match the bacterial DNA sequence obtained from a given specimen to published gene sequences that are available from scientific databases. According to one recent estimate, DNA sequencing information is available for 9,800 bacterial species.[10] These databases are continually updated as new species are identified.

Evidence from healthy individuals indicates that the kinds of bacteria found at specified sites vary widely among people. For example, oral swabs taken from two people will yield differences in the composition—the types and amounts—of bacterial species in the sample.[11] This variation makes it difficult to identify the "ideal" bacterial community needed for optimal health. The structures of various microbial communities also vary widely within an individual. For example, vaginal and oral swabs taken from the same person will yield even greater differences, indicating that each body site has a distinct composition that likely relates to the functions of the microbes at that site.[11]

GI MICROBIOTA

The microbiota in the gut inhabit the entire GI tract from the oral cavity to the rectum. There is increasing evidence to support early findings indicating that colonization of the GI tract begins in utero.[12] A number of studies have isolated small amounts of nonpathogenic bacteria from meconium and placental specimens.[12-16] That said, such exposure before birth is necessarily limited. The initial composition of the GI tract's microbial communities is primarily influenced by the birth process and events shortly afterward. At birth, infants come into physical contact with microbial communities in the birth canal during vaginal deliveries and on the skin of hospital staff and parents during cesarean deliveries.[17,18] The mode of microbial exposure at birth, combined with other early life factors, contributes to varying GI tract colonization patterns among infants.[19,20]

The other factors that influence the development of the GI microbiota include the feeding method (breast

or bottle); medications given during the neonatal and infancy periods; and exposures in the external environment, such as via siblings.[19, 21-24] Backhed and colleagues found that exclusively breastfed infants harbored more gut bacteria that are often used as probiotics.[19] Other researchers have found that formula-fed infants have a higher abundance of *Clostridium difficile* in the GI tract.[22, 24] *C. difficile*, an opportunistic pathogen that can cause severe gastric disturbances, has also been associated with later development of allergies.[25]

Not surprisingly, infants treated with antibiotics show differences in the bacterial composition of the GI tract when compared with untreated infants.[19, 23, 24] The implications of this are not well understood. But findings from one mouse study suggest that composition of gut microbiota at an early age may affect the development of immune function and metabolic function.[26] And it's known that, in humans, the gut mucosal lining serves as a critical component of the immune system and as a sensor and regulator of the GI microbiota. Through early exposure to nonindigenous microbes, pattern receptors in or on this lining learn to differentiate between commensal and pathogenic bacteria.[27, 28] This in turn permits activation of the immune defenses when necessary. Thus, establishing the constituents of the GI microbiota early in life is critical; if this process is disrupted, there may be lasting detrimental effects.[18, 27]

The composition of a child's GI microbiota generally resembles that of an adult's, once breastfeeding ceases and solid food dominates the diet—a transition that typically occurs between the ages of one and three years.[19, 21, 29] It's been estimated that, by adulthood, there are more than 1,000 different species of bacteria in the GI tract, depending on dietary intake, environmental exposures such as antibiotics, and physiologic maturation.[3, 4, 30, 31] In general, an adult's GI microbiota contains species belonging to four major bacterial phyla: Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. Collectively, bacteria from these four phyla constitute more than 90% of the adult GI microbiota and reside mainly in the large intestine.[32] The large intestine has a higher density of microbes because content passes through the intestine more slowly, allowing microbes more time to multiply. Furthermore, compared with the small intestine, the large intestine characteristically has a more neutral-to-alkaline pH, providing a more hospitable environment for many microbes.[31]

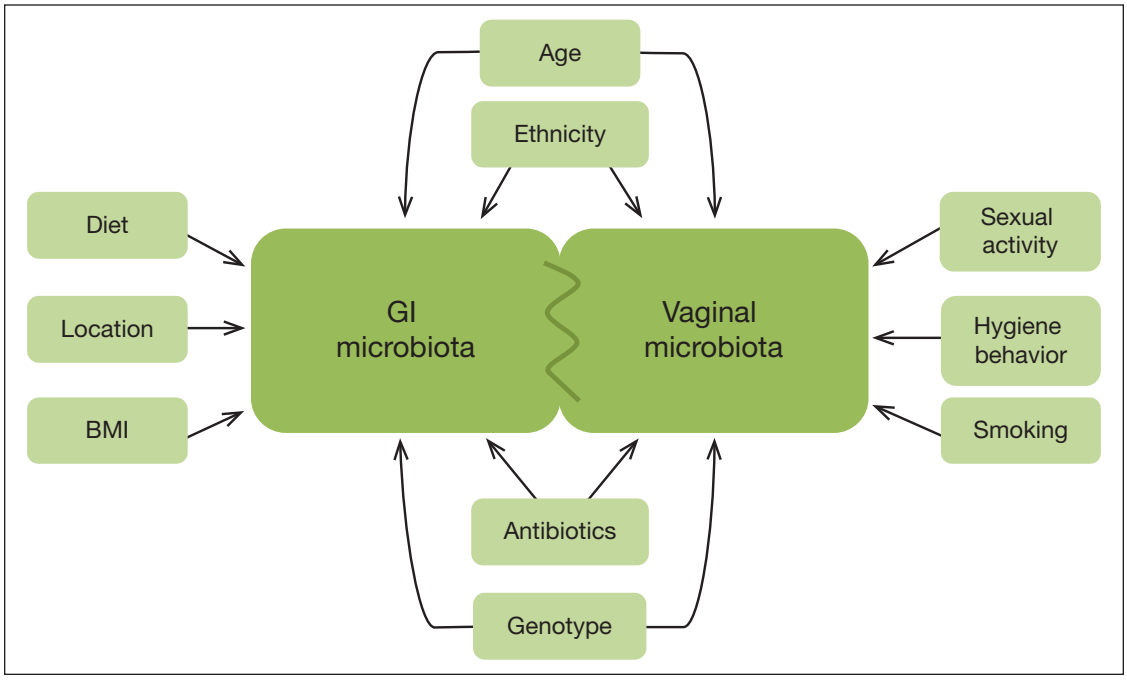
Increasing evidence suggests that the kinds of bacteria found in the large intestine can influence physiologic functions, including immunomodulation and mood regulation.[33, 34] One known mechanism of influence involves metabolites of the GI microbiota that result from the fermentation of fibrous foods, a process that breaks down complex organic compounds into smaller ones.[20, 35, 36] Metabolites, such as the short-chain fatty acids (SCFAs) butyrate, acetate, and propionate, influence physiologic function by binding to various human cell receptors. For example, when SCFAs bind to an immune cell receptor, they can regulate inflammatory pathways involved in conditions such as Crohn's disease and bacterial vaginosis.[37-39] Recent study findings indicate that SCFAs also regulate the production of certain neurotransmitters (including serotonin), which influence cognition, mood, and behavior; they do so by initiating the process involved in their biosynthesis.[40-42]

Metabolites produced by the GI microbiota also serve as a vital nutrient supply for the epithelial cells in the colon.[43] Those cells form the mechanical barrier that blocks microbes from crossing into the bloodstream, thereby protecting the host against infection. And GI microbiota support human physiology by synthesizing vitamins from food. Certain microbes possess genes not found in human DNA that encode enzymes necessary to produce vitamins, including the B vitamins and vitamin K.[44] Research suggests that such synthesis depends both on the types of microbes present and on adequate intake of the complex carbohydrates that serve as substrates for microbial metabolism.[44]

Multiple factors influence the composition of GI microbiota, including demographic factors and health behaviors. (For a graphic overview of factors influencing both the GI and vaginal microbiota, see Figure 1.) There is some evidence to suggest that diet may have the greatest effect,[45] and that changes can occur rapidly. One study, conducted in mice given "humanized" gut ecosystems, found that switching from a low-fat, plant-rich diet to a high-fat, high-sugar Western diet shifted the composition of the GI microbiota within a single day.[46] Similarly, a small study among humans found that consuming a diet emphasizing animal-based foods (such as meat, eggs, and cheese) resulted in increased levels of bile-tolerant microbes and decreased levels of Firmicutes, which metabolize dietary plant sugars, within days.[47] Longer-term dietary patterns also influence GI microbiota. De Filippo and colleagues compared the GI microbiota of rural African children, who typically consume a low-fat, low-protein, high-fiber diet, with those of European children, who typically consume a high-fat, high-protein, low-fiber diet, and found significant differences.[48] For example, Bacteroidetes species, which are involved in the fermentation of complex carbohydrates, were more abundant in the GI microbiota of the African children than the European children (58% and 22%, respectively). Firmicutes species, which are often associated with obesity, were more abundant in the GI microbiota of the European children than the African children (64% and 27%, respectively).

Taken together, such findings strongly suggest that the structure of the GI microbiota is closely tied to

Figure 1. Factors Influencing GI and Vaginal Microbiota



BMI = body mass index; GI = gastrointestinal.

the many functions of the GI tract, and that GI microbiota are unique when compared with microbiota found elsewhere in or on the human body.

VAGINAL MICROBIOTA

The vaginal microbiota includes all microbes residing in the vagina and the ectocervix. For decades it's been known that lactobacilli are integral members of the vaginal microbiota.[49] Lactic acid produced by lactobacilli contributes to the acidic environment of the vagina.[50] The low vaginal pH (typically 3.5 to 4.5) enhances the protective function of vaginal microbiota by preventing pathogenic overgrowth and subsequent infection.[51]

In recent years, 16S rRNA gene profiling has demonstrated that the vaginal microbiota transform over the course of the female life cycle in response to hormonal changes that occur during puberty, pregnancy, and menopause.[52, 53] A small number of studies have focused on the vaginal microbiota of adolescent girls; these have found that as girls progress through the stages of puberty, lactobacilli become more abundant, even before menarche.[54, 55] Similarly, few studies have focused on the vaginal microbiota in postmenopausal women. But there is evidence that, after menopause, lactobacilli become less abundant as estrogen levels decrease.[52, 56]

Much more is known about the vaginal microbiota of women of reproductive age. Ravel and colleagues demonstrated that vaginal microbial communities in this population were highly variable in composition but could be classified into five general types.[57] Distinct *Lactobacillus* species dominated four of the five types. The fifth type contained fewer *Lactobacillus* species, more diverse arrays of bacterial anaerobes, and could often be subdivided further. Other studies found similar results in diverse samples of women.[52, 58, 59]

Many researchers studying the vaginal microbiota have concluded that its composition varies widely among women and that no single composition typifies health or disease. That said, there is evidence that vaginal dysbiosis, an imbalance of the vaginal microbiota characterized by potentially harmful combinations of certain types and levels of bacteria, is common in women of reproductive age.[57, 60]

Vaginal dysbiosis includes bacterial vaginosis and aerobic vaginitis; in the United States, up to 50% of women of reproductive age may be affected.[61] Potential adverse effects include vaginal discomfort, unwanted odor, and itching; increased risk of preterm birth and postpartum infection; poor outcomes in future pregnancies; and increased incidence of sexually transmitted infections, including HIV.[62-67] No single microbial community profile is associated with bacterial vaginosis or other vaginal dysbioses, but these conditions are typically characterized by a paucity of lactobacilli and elevated vaginal pH (greater than 5).

Factors correlated with bacterial vaginosis and other changes in vaginal microbiota have been well

documented.[63, 65, 68, 69] Hygienic and sexual practices that have been linked to vaginal dysbiosis include douching, using vaginal lubricants, and having a greater number of sexual partners.[65, 68, 69] Research indicates that certain bacterial species are generally more prevalent during dysbiosis.[70] Yet bacteria associated with bacterial vaginosis are sometimes present in moderate amounts in women with no accompanying signs or symptoms of illness.[57, 60] This suggests that other factors, such as genetics or immune system interactions, may be relevant in progression to a symptomatic or harmful state, but at this writing such factors remain unexplored.

In addition to providing protection against infection, the vaginal microbiota contribute to neonatal GI tract colonization during birth.[17, 19] It's imperative that we learn more about the structure and functions that vaginal microbiota play during pregnancy, and more researchers are including pregnant women in their studies. Thus far, study findings indicate that the types of microbes present may influence the length of pregnancy, the incidence of miscarriage, and fertility.[66, 67, 71] For example, a recent meta-analysis reported increased odds of infertility in women with bacterial vaginosis.[72]

The kinds of bacteria found in the large intestine may influence physiologic functions, including immunomodulation.

Taken together, the evidence shows that the vaginal microbiota serve two major purposes over the course of the female life cycle: prevention of infection and neonatal GI tract colonization. Alterations in composition that result in dysbiosis can have lasting, potentially devastating effects.

NURSING IMPLICATIONS

Given the mounting evidence for how the human microbiome influences health, it's crucial that nurses have a basic understanding of this microbiome and can apply it when providing care. Although individuals will display vast differences in the kinds of bacteria that make up the various communities in the GI and reproductive tracts, commonalities do exist. Much remains to be learned, and further research exploring the structures and functions of the GI and vaginal microbiota is warranted. The evidence may provide insights into how to create more effective interventions for treating illness and promoting health. As frontline caregivers and patient educators, nurses can both contribute to such research and incorporate the latest findings into patient care.

It's important to remember that many modifiable factors contribute to vaginal dysbiosis, including hygienic and sexual practices that alter microbial composition in the vagina. Nurses can provide education aimed at decreasing potentially harmful behaviors in high-risk populations. For example, the practice of douching is still common in certain cultures.[73] Yet studies have shown that douching is associated with an increased prevalence of bacterial vaginosis.[65, 74] Women presenting with bacterial vaginosis should be asked about douching habits, and provided with education on safer hygienic practices as warranted.

The stability of the vaginal microbiota is crucial during pregnancy because of the role that vaginal delivery plays in establishing an infant's GI microbiota. It's imperative for perinatal nurses to understand that common practices such as antibiotic administration and lubricant use during labor and delivery can alter the composition of the vaginal microbiota, leading to suboptimal colonization of the newborn.[68, 75] Perinatal nurses can minimize the number of vaginal examinations involving lubricants during labor. For women given antibiotics, nurses can emphasize the increased need for other actions associated with healthier neonatal GI colonization, such as immediate and longer-term breastfeeding.

Perinatal nurses should also know that cesarean-born infants have different GI tract colonization patterns than vaginally born infants,[19, 76] and may be at higher risk for adverse outcomes such as asthma and childhood obesity.[17, 77, 78] One recent study by Dominguez-Bello and colleagues explored the potential for inoculating cesarean-born infants with their mother's vaginal fluids.[79] While the early results were promising—the researchers reported "partial restoration" of vaginal microbes into the infants' microbial communities—further research is needed before this intervention can be introduced into the clinical setting. There is also evidence that it's the cessation of breastfeeding, rather than the introduction of solid foods, that influences the development of the GI microbiota.[19] Backhed and colleagues found that, compared with infants still being breastfed, those who had stopped breastfeeding had gut microbiota that more closely resembled those found in adults.[19] The researchers noted that such bacteria have lasting effects on essential processes such as metabolism, and may play a role in brain development.

In both children and adults, antibiotic administration and unhealthy eating behaviors can induce perturbations in the GI microbiota that may increase the risk of developing metabolic syndrome or autoimmune diseases. Nurses need to keep up with the current research in these areas. For example, various recent studies have investigated the use of prebiotics, probiotics, and fecal transplantation in treating inflammatory bowel disease, diabetes, and obesity.[80, 81]

Fibrous foods are the main source of prebiotics, while bifidobacteria and *Lactobacillus* spp. are commonly used as probiotics. But differences in individual baseline microbial communities must be taken into account; commercially available supplements might not contain the right microbes for a particular person. Although at this writing neither the optimal "healthy" microbes and microbial communities nor their mechanisms have been fully identified, fecal transplantation using specimens from healthy donors has reportedly been shown to alleviate symptoms of *C. difficile* infection by restoring the balance of an altered microbial community.[82] More research investigating indications for and methodologies of fecal transplantation is currently under way.[83]

There is no doubt that the human microbiome profoundly influences human health, and the body of evidence in this area is growing rapidly. In order to provide complete, evidence-based care, it's essential for nurses in all settings to follow practices that incorporate what we know about the microbial communities that inhabit our bodies. ▼

For eight additional continuing nursing education activities related to the topic of genomics, go to www.nursingcenter.com/ce.

Katie Gresia McElroy is an assistant professor in the Department of Family and Community Health at the University of Maryland School of Nursing, Baltimore, where Mary Regan is an associate professor in the Department of Organizational Systems and Adult Health. Seon-Yoon Chung is an assistant professor at Illinois State University Mennonite College of Nursing, Normal. *This article was supported in part by unrestricted educational grants from the National Institutes of Health (NIH) as follows: the National Institute for Nursing Research, grant number R01NR014826; and the Eunice Kennedy Shriver National Institute of Child Health and Human Development, grant number 1F31HD080360. The content is solely that of the authors and does not necessarily represent the official views of the NIH.* *Contact author: Katie Gresia McElroy, mcelroy@son.umaryland.edu.* *The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.*

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