JCCC Honors Journal

Volume 9
Issue 2 *Spring 2018*

Article 3

2018

The Lifelong Impact of the Neonatal Microbiome

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Abstract

Nurses have a critical role in patient health outcomes. Beyond providing essential care, nurses are responsible for educating patients so they are able to make well-informed decisions to achieve optimal health. Throughout our training, we are consistently reminded of the importance of patient education. When a diagnosis is made, nurses are responsible for teaching the patient how to respond in order to best manage their condition. While this will always be a vital component of nursing, another approach to patient education is preventing disease. Research has proven that the human microbiome is essential to health and disease prevention, yet its significance continues to be overlooked in the medical community. In order to best serve our patients, it is imperative that nurses are informed of the importance of a healthy human microbiome and the lifelong risks associated with its neglect.

Cover Page Footnote

The faculty mentor for this Honors contract was Professor Angela Sears, Nursing.

Nurses have a critical role in patient health outcomes. Beyond providing essential care, nurses are responsible for educating patients so they are able to make well-informed decisions to achieve optimal health. Throughout our training, we are consistently reminded of the importance of patient education. When a diagnosis is made, nurses are responsible for teaching the patient how to respond in order to best manage their condition. While this will always be a vital component of nursing, another approach to patient education is preventing disease. Research has proven that the human microbiome is essential to health and disease prevention, yet its significance continues to be overlooked in the medical community. In order to best serve our patients, it is imperative that nurses are informed of the importance of a healthy human microbiome and the lifelong risks associated with its neglect.

In order to utilize the microbiome in disease prevention, nurses need to comprehend precisely what it is and appreciate its role in the human body. In 2008, the Human Microbiome Project was established, and research has focused on the understanding the human microbiome and its role in health and disease (Peterson, 2009). This study has provided a standardized reference for all subsequent studies for microbiome research. The human microbiome is a "community of microorganisms (bacteria, fungi, viruses) that reside upon and within the human body" (Wright & Starkweather, 2015). A healthy microbiome contains a high diversity of beneficial microbial species and has an ability to resist change in times of physiological stress. On the contrary, an unhealthy microbiome has a significantly lower species diversity, with far fewer beneficial microbes, and at times includes harmful microbes, known as pathobionts (Chan & Gibson, 2013, p. 33). Although microbiota inhabit every niche of the human body, researchers have identified a unique "core" microbiome inhabiting the mouth, skin, gut, urogenital tract, and vagina (Gevers et al., 2012). The main phyla present in the human microbiome are Firmicutes, Bacterioidetes, Actinobacteria, Proteobateria, Fusobacteria, Spirochaetae and Verrucomicrobia (Chan & Gibson, 2013, p. 29). Periods of unhealthy microbial composition are referred to as "dysbiosis" (Wright & Starkweather, 2015), demonstrating an imbalance in microbiota species or proportions that leads to altered health outcomes. Microbiomes vary with each individual and are constantly changing.

The microbiome has several critical roles in human health and immunity. Vaginal microbiota can affect fertility, length of pregnancy, and miscarriage (Regan et al., 2017). An altered maternal microbiome has been associated with preterm labor (Wright & Starkweather, 2015). Researchers have identified preterm birth in the U.S. as the leading cause of infant morbidity and mortality (Ollberding et al., 2016). Countless studies have identified microbiome dysbiosis to be directly associated with poor pregnancy outcomes.

There has been a great focus on the microbiome and the human gut. "Bacterial colonization of the gut plays a major role in postnatal development and maturation of key systems that have the capacity to influence central nervous system (CNS) programming and signaling, including the immune and endocrine systems." (Moloney et al., 2014). Another study suggests improper communication between the gut microbiome and the innate immune system acts as a catalyst of complex disease by stating the "intestinal microbiome is a signaling hub that integrates environmental inputs, such as diet, with genetic and immune signals to affect the host's metabolism, immunity and infection" (Thaiss et al., 2007). Over time, more and more studies have identified the relation between the microbiome and poor immune function. More recently, researchers have solidified the concept of a commensal relationship between human microbiota and the immune response, in which both are critical for optimal health. "A balanced relationship between the host's microbiota and the immune system is crucial for a homeostatic response toward pathogenic attack and to prevent aberrant inflammation" (Tamburini et al., 2016). Any alteration to either the microbiome or the immune response will negatively impact the body's ability to fight off invading pathogens and could result in altered inflammatory response. Nutritionally, microbial imbalance can lead to constipation, diarrhea, obesity, malabsorption, malnutrition, failure to thrive, necrotizing enterocolitis or growth and developmental delays (Wright & Starkweather, 2015, p. 307). Dysbiosis can have serious consequences for neonatal life.

In addition to early life outcomes, an altered microbiome increases risks for disease throughout infancy and childhood. Dysbiosis has been identified in many patients diagnosed with asthma, celiac disease, and many metabolic disorders (Mueller et al., 2015). Numerous studies have linked an altered microbiome to behavior, mood, and mental health conditions. A link between the gut microbiota and brain development has been identified; specifically, how dysbiosis can impact neurodevelopment, and subsequently, alter motor, cognitive and social-emotional development (Heijtz, 2016). This study also associates undeveloped microbiomes to autism, depression, and anxiety. Although countless theories exist, researchers are trying to prove the precise etiology for dysbiosis associated with mental health conditions and disease. However, findings show a vast majority of those diagnosed with such have an imbalanced microbiota.

When the microbiome is malformed, immune function is compromised and the inflammatory response is altered, which can lead to chronic disease later in life. Research has associated dysbiosis with countless conditions and diseases. A prominent study in 2013 established a clear relation between dysbiosis and several conditions and diseases, including inflammatory bowel disease, colorectal cancer, obesity, atherosclerosis, diabetes, and nonalcoholic fatty liver disease (Chan & Gibson, 2013). Research specific to the oral microbiome has linked an imbalanced microbiota to cardiovascular disease, stroke, and even Alzheimer's disease (Cobb et al. 2017). There have been countless studies that have correlated dysbiosis with serious health consequences throughout the lifespan.

Up until the past few years, it was believed that the development of the neonatal microbiome didn't begin until after birth or rupture of membranes. Moreover, in the past, microbial DNA found in the intrauterine components, such as the placenta, umbilical cord blood, fetal membrane, and amniotic fluid, were considered to be the remnants of infection during fetal development (Tamburini et al., 2016). However, newer research shows evidence of microbial presence in the placenta, umbilical cord, amniotic fluid, and meconium in majority of healthy pregnancies, with no known infection (Mueller et al., 2015). Numerous studies have confirmed the major impact of neonatal microbiome development to be mode of delivery, with a clear distinction between vaginal delivery compared to cesarean. Vaginal delivery establishes a neonatal microbiome that resembles maternal vaginal microbiota rich in beneficial Lactobacillus, which is much more favorable than cesarean delivery microbiome that mimics the skin microbiota of the neonate's mother and involved healthcare workers and the surrounding hospital environment (Heijtz, 2016). While it's unknown precisely how long subsequent development of the microbiome in cesarean born infants takes to mimic that of vaginally born infants, studies have suggested it can take up to seven years (Mueller et al., 2015). Considering the consequences of risks associated with dysbiosis, it would be ill-advised to promote elective cesarean birth.

In addition to mode of delivery, diet is a critical component that impacts neonatal microbiota. Maternal gut microbiota transferred to the infant through breastmilk positively impacts neonatal microbiome development (Fernández et al., 2012). In addition, breastmilk provides immunoglobulins and antibodies to protect the infant from invading pathogens and subsequent microbiota imbalances. Breastmilk acts as a natural prebiotic source to promote the development of beneficial microbes and nourishment for their growth (Ross et al., 2017). Studies have shown that formula fed infants harbor a greater abundance of pathogenic microbiota, which can lead to critical gastric disturbances during infancy and allergies later in life (Regan et al., 2017). In addition to using formula, introduction of solid foods too early in infancy can alter the neonatal intestinal microbiota (Mueller et al., 2015). Research proves breastmilk is the best choice to promote the neonatal microbiome and prevent disease.

Antibiotic use during pregnancy, labor, or early life can negatively alter the neonatal microbiome. Maternal antibiotic use in labor, as well as in neonates in the postnatal period, has been linked to dysbiosis in neonates (Bertelsen et al., 2016). Antibiotic use in premature neonates are more likely to have a less diverse microbiome and are at a higher risk of infection and mechanical ventilation (Wright & Starkweather, 2015). Additionally, it is suggested that antibiotic usage in neonates increases the risk of developing inflammatory conditions, such as IBS, asthma, milk allergy, or Type II Diabetes (Tamburini et al., 2016). Antibiotic use clearly alters microbiota abundance and can easily lead to dysbiosis, increasing the risk for altered health outcomes.

Since research strongly suggests fetal exposure to maternal microbiota during pregnancy, promoting a healthy microbiome in the prenatal period is warranted. Several studies have suggested maternal comorbidities, such as diabetes, eczema, and celiac disease, and subsequent treatments of such, can alter the neonatal microbiome and lead to disease later in life (Wright & Starkweather, 2015). This study also suggests maternal diet can impact fetal microbial exposure, and that maternal obesity can lead to neonatal dysbiosis. Psychological stress during pregnancy can alter the mother's microbiome, and subsequently could negatively impact neonatal microbiota development, leading to undesirable mental health outcomes in childhood and beyond (Heijtz, 2016). Behaviors that promote a healthy microbiome in mothers, such as a high-fiber, low-fat diet, along with proper hygiene, rest, and exercise, will provide superior microbial exposure to the developing fetus and neonate.

When cesarean birth, formula feeding, and antibiotic use are unavoidable, alternative methods of providing beneficial microbes is necessary. Cesarean births in the U.S. are at an all-time high, quite possibly since some mothers elect to have a c-section when vaginal delivery is still a realistic and safe option. Knowing the negative impact of neonatal microbiome development, vaginal delivery is the optimal choice. However, when vaginal delivery is not possible or is too risky, interventions can help promote optimal neonatal microbiota. Waiting to administer maternal prophylactic antibiotics for cesarean birth until immediately after the neonate has been separated from the placenta will prevent unnecessary exposure, and avoid the destructive impact to the neonate's microbiome. In addition, inoculating the neonate with a swab of maternal vaginal fluids immediately after birth, provides beneficial microbial exposure that would otherwise take years to develop in the offspring (Regan et al., 2017). Breastmilk is a critical restorative component for cesarean delivered neonates (Fernández et al., 2012). However, when providing breastmilk isn't possible, formula supplemented with prebiotics is the next best choice (Bertelsen et al., 2016). Administering probiotics during infancy can help provide key bacteria for the developing microbiome (Heijtz, 2016). Avoiding damaging antibiotic exposure, along with promoting inoculation, breastmilk, and use of probiotics can stimulate healthy neonatal microbiome development when more beneficial methods aren't possible.

Other contributing factors can alter microbiome development after birth, including hygiene, diet, and environmental exposures. The neonate's first bath can negatively impact the natural protective barrier in place at birth. The vernix protects against invading pathogens, and therefore, should only be wiped off at birth, and not washed off with soap or water. In addition, parents and caregivers should practice good hand-hygiene to reduce the risk of infection. "The 'hygiene hypothesis' proposes that reduced microbial exposure leads to an exaggerated adaptive immune response and reduced tolerance" (Bertelsen et al., 2016). Environmental exposures starting in infancy, such as dust and animals, can provide beneficial microbes to the developing microbiome. Children raised on farms have more diverse and abundant microbiota (Tamburini et al., 2016). Cohabitating with non-blood relatives and attending daycare are both environments that provide additional chronic exposure to different microbial species, leading to a more diverse microbiome (Tamburini et al., 2016). Exposing the infant to beneficial microbes, while also preventing infection, is a critical approach to supporting microbiome development.

Microbial supplementation is beneficial the microbiome. Maternal consumption of probiotics during pregnancy and while breastfeeding impacts the neonatal microbiome (Mueller et al., 2015). Lactobacillus reuteri supplementation to mothers towards the end of pregnancy, and subsequently, to the offspring until the age of 12 months, decreases levels of the infant's IgE antibodies to food allergens by two years of age (Mueller et al., 2015). Some studies suggest probiotic administration to breastfeeding mothers and formula fed infants could lower the incidence of excessive infant crying, as well as the number of episodes of infant colic (Bertelsen et al., 2016). Prebiotics, are non-digestible food ingredients that promote beneficial microbes, by increasing the abundance of microbes or by improving existing microbial performance. Breastmilk is naturally rich in prebiotics, but cow's milk provides virtually none; formula enhanced with prebiotics may result in a microbiomes that more closely mimic that of breast-fed infants. (Bertelsen et al., 2016). Countless studies have identified benefits of prebiotic and probiotic supplementation to promote neonatal development and infection prevention.

The most effective nursing intervention to promote neonatal microbiome development is through patient education. Proactively, a focus should be placed on maternal health and microbiota homeostasis. Patients should be made aware of the impact their current health and medications could have on the developing fetus. Unless otherwise indicated, the following recommendations should be advised: eating a balanced high-fiber, low-fat diet, consistently exercising, getting adequate sleep, and seeking help for mental health & stress management, if necessary. Patients should be advised to avoid overuse of antibiotics, and to consider probiotic and prebiotic therapy with their provider when antibiotic use is absolutely necessary. Pregnancy can bring about a lot of changes and increased responsibility. Educating partners and support members could further promote the best possible outcome for maternal and fetal well-being.

Gestation age and mode of delivery can severely impact neonatal microbiome development. Educating patients to avoid elective cesarean-sections and promoting full term pregnancies, unless otherwise indicated, is key. When cesarean is unavoidable, mom's should be informed of the health promoting benefits of immediate inoculation to their newborn baby and antibiotic therapy should be administered only after the neonate is born. Breastfeeding is the most beneficial diet in almost all neonates; when formula is necessary, prebiotic and probiotic supplementation should be considered. Parents should be informed of the benefit of the vernix, and to avoid soap and water baths immediately after birth. Hygiene education is important, and an emphasis on hand-hygiene should be presented to all caregivers. It's important to avoid infection by limiting exposure to others with contagious conditions, and also by preventing skin breakdown by routinely changing diapers every two hours, or more frequently when soiled. Encouraging maternal rest and stress management continue to be important components to promote.

During infancy and beyond, nurses should encourage healthy microbial exposure, such as interacting with other people and fostering play with animals and dirt. An emphasis should be placed upon the benefit of extended breastfeeding and avoidance of introducing solid foods too early. Mothers that breastfeed should continue to support their own microbiome and overall health. After infancy, the diet should contain adequate amounts of fiber to support the microbiome. As always, overuse of antibiotics should be avoided. When microbiota homeostasis is compromised, prebiotic and probiotic therapy should be considered.

Patient health outcomes can be greatly influenced through nursing interventions. The microbiome is modifiable. Nurses can significantly impact patients through education regarding the importance of establishing & maintaining a healthy microbiome, which can dramatically improve pregnancy outcomes and reduce the risk of disease across the lifespan. Providing information to restore microbial homeostasis when dysbiosis occurs is an additional nursing intervention of significant impact. Through knowledge, compassion, and perseverance, nurses have the power to impact patient health and quality of life.

References

Bertelsen, R. J., Jensen, E. T., & Ringel-Kulka, T. (2016). Use of probiotics and prebiotics in infant feeding. Best Practice & Research Clinical Gastroenterology, 30(1), 39-48. doi:10.1016/j.bpg.2016.01.001

Chan, Y. K., Estaki, M., & Gibson, D. L. (2013). Clinical consequences of diet-induced dysbiosis. *Annals of Nutrition & Metabolism, 63*, 28-40. doi:http://dx.doi.org.ezproxy.jccc.edu/10.1159/000354902

Cobb, C. M., Kelly, P. J., Williams, K. B., Babbar, S., Angolkar, M., & Derman, R. J. (2017). The oral microbiome and adverse pregnancy outcomes. International Journal of Women's Health, 9, 551+. Retrieved from http://link.galegroup.com.ezproxy.jccc.edu/apps/doc/A531979424/HRCA?u=jcl_jccc&sid=HRCA&xid=4bd487f9

Fernández, L., Langa, S., Martín, V., Maldonado, A., Jiménez, E., Martín, R., & Rodríguez, J. M. (2013). The human milk microbiota: Origin and potential roles in health and disease. Pharmacological Research, 69(1), 1-10. doi:10.1016/j.phrs.2012.09.001

Gevers, D., Knight, R., Petrosino, J. F., Huang, K., McGuire, A. L., Birren, B. W., ...Huttenhower, C. (2012). The Human Microbiome Project: a community resource for the healthy human microbiome. PLoS Biology, 10(8). Retrieved from http://link.galegroup.com.ezproxy.jccc.edu/apps/doc/A302114408/AONE?u=jcl_jccc&sid=AONE&xid=e8083fd8

Heijtz, R. D. (2016). Fetal, neonatal, and infant microbiome: Perturbations and subsequent effects on brain development and behavior. *Seminars in Fetal and Neonatal Medicine, 21*(6), 410-417. doi:10.1016/j.siny.2016.04.012

Moloney, R. D., Desbonnet, L., Clarke, G., Dinan, T. G., & Cryan, J. F. (2014). The microbiome: Stress, health and disease. Mammalian Genome, 25(1), 49-74. doi:10.1007/s00335-013-9488-5

Mueller, N. T., Bakacs, E., Combellick, J., Grigoryan, Z., & Dominguez-Bello, M. G. (2015). The infant microbiome development: Mom matters. Trends in Molecular Medicine, 21(2), 109-117. doi:10.1016/j.molmed.2014.12.002

Ollberding, N. J., Völgyi, E., Macaluso, M., Kumar, R., Morrow, C., Tylavsky, F. A., & Piyathilake, C. J. (2016). Urinary microbiota associated with preterm birth: Results from the conditions affecting neurocognitive development and learning in early childhood (CANDLE) study. PloS One, 11(9), e0162302. doi:10.1371/journal.pone.0162302

Peterson, J., Garges, S., Giovanni, M., McInnes, P., Wang, L., Schloss, J. A., . . . NIH HMP Working Group. (2009). The NIH human microbiome project. Genome Research, 19(12), 2317.

Regan, M., Chung, S., & McElroy, K. G. (2017). Health and the human microbiome: A primer for nurses. American Journal of Nursing, 117(7), 24.

Ross, R. P., Ryan, C. A., Stanton, C., & Watkins, C. (2017). Microbial therapeutics designed for infant health. Frontiers in Nutrition, 4 doi:10.3389/fnut.2017.00048

Tamburini, S., Shen, N., Wu, H. C., & Clemente, J. C. (2016). The microbiome in early life: Implications for health outcomes. Nature Medicine, 22(7), 713-722. doi:10.1038/nm.4142

Thaiss, C. A., Zmora, N., Levy, M., & Elinav, E. (2016). The microbiome and innate immunity. Nature, 535(7610), 65-74. doi:10.1038/nature18847

Wright, M. L., & Starkweather, A. R. (2015). Antenatal Microbiome. Nursing Research, 64(4), 306-319. doi:10.1097/nnr.0000000000000101