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The Maternal Infant Microbiome: Considerations for Labor and Birth

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Abstract

The human microbiome plays a role in maintaining health, but is also thought to attenuate and/or exacerbate risk factors for adverse maternal-child health outcomes. The development of the microbiome begins in utero, however factors related to the labor and birth environment have been shown to influence the initial colonization process of the newborn microbiome. This “seeding” or transfer of microbes from the mother to newborn may serve as an early inoculation process with implications for the long-term health outcomes of newborns. Studies have shown that there are distinct differences in the microbiome profiles of newborns born vaginally compared to those born by cesarean. Antibiotic exposure has been shown to alter the microbial profiles of women and may influence the gut microbial profiles of their newborns. Considering that the first major microbial colonization occurs at birth, it is essential that labor and birth nurses be aware of factors that may alter the composition of the microbiome during the labor and birth process. The implications of various activities and factors unique to the labor and birth environment that may influence the microbiome of women and newborns during the labor and birth process (e.g. route of birth, antibiotic use, nursing procedures) are presented with a focus on the role of labor nurses and the potential influence of nursing activities on this process.

Keywords

pregnancy; vaginal microbiome; parturition; cesarean birth; pregnancy complications

Introduction

Living on and within each person are complex ecological communities of microbes, or microbiota (Turnbaugh et al., 2007). Consisting of bacteria, fungi, and archaea, these microbiota live in relative symbiotic harmony with their hosts. The collective genomes of these microbes are known as the microbiome. Scientists now understand that each person's unique collection of traits are actually the result of complex interactions between human and microbiota processes, creating one composite, 'human supraorganism' (See table 1). The symbiotic relationship between humans and microbes has evolved over millions of years, allowing each to thrive in their biophysical environment. Rapid changes in human lifestyles over the past 100 years, including profound alterations in modern-day birthing practices (Epstein, 2010), have the potential to transform our microbiome with unknown implications for health and predisposition to disease (Cho & Blaser, 2012).

The first major microbial colonization of newborns occurs at birth, when newborns are 'seeded' with their mothers' microbiota (Backhed et al., 2015). Medicalization of birth in many developed nations has changed the quality and quantity of contact between mothers and babies, altering this initial microbiome composition and formation (Backhed et al., 2015; Epstein, 2010). The newest evidence on factors in the labor and birth environment (e.g. route of birth, vaginal exam frequency, antibiotic use) that may influence the maternal and newborn microbiome, and identify relevant practice implications and considerations for labor and birth nurses is presented.

Prenatal Considerations

Colonization and establishment of the newborn microbiome is a process that likely begins prior to birth, as microbes have been isolated from the placenta, fetal membranes, amniotic fluid, and umbilical cord blood (Aagaard et al., 2014; Oh et al., 2010). Although traditionally the intrauterine environment has been considered sterile, a recent study investigating the microbial composition of placental basal plates (peripheral surface of the placenta on the maternal side) identified both gram positive and gram negative bacteria in 54% of those giving birth preterm and 26% of those giving birth at term (Stout et al., 2013). Similarly, Aagaard et al. (2014) sequenced the bacterial species of placentas following normal term pregnancies and found a variety of bacteria in low abundance including *Escherichia coli*, *Prevotella tannerae*, and *Bacteroidetes*, suggesting that the placenta may harbor its own commensal flora. Although the presence of bacteria in the intrauterine environment has traditionally been associated with perinatal complications such as preterm birth, (Gregory, 2011), future research is needed to explore the function of this newly discovered microbiome, its role in perinatal health processes, and the initial establishment of the newborn microbiome.

The mechanisms by which bacteria translocate into the intrauterine cavity are not yet clear. Several theories have been proposed including hematogenous translocation from the oral cavity and gastrointestinal (GI) tract, supported by the finding that non-pathogenic microbiota similar to those found in the oral cavity (e.g. *Firmicutes*, *Proteobacteria*) and GI tract (e.g. *Enterococcus*, *Streptococcus*) have been isolated from the placenta and amniotic

cavity (DiGiulio, 2012; Solt, 2015). Vaginal microbes have also been isolated in intrauterine samples (Witkin, 2014) suggesting that organisms from the vagina may ascend into the intrauterine cavity from the vaginal canal. Further research is needed to explore a potential prenatal maternal-fetal exchange of microbes.

The gut and vaginal microbiomes are the primary sources from which the initial transfer of microbes to the newborn is likely to occur, and research suggests that pregnancy may influence these maternal microbiome environments (Nuriel-Ohayon, Neuman, & Koren, 2016). A recent study of 24 pregnant women between 18 and 40 weeks sought to characterize the composition and dynamics of the vaginal microbiome during pregnancy and found that species diversity and richness decreased throughout pregnancy with an overall dominance of *Lactobacillus* species as well as *Clostridiales*, *Bacteroidales*, and *Actinomycetales* orders (Aagaard et al., 2012). These findings suggest that the microbiome signature of pregnancy is dynamic and changes throughout gestation although the factors that promote such changes are not yet fully understood (Aagaard et al., 2012). Gut microbiota in pregnant women with gestational diabetes also appear to change significantly across gestation, with an increased abundance of disease associated microbes including *Actinobacteria* and *Proteobacteria* in the third trimester (Koren et al., 2012). Germ-free mice, when inoculated with these third trimester bacterial samples, demonstrated a greater presence of inflammation, increased fat storage, and insulin resistance (Koren et al., 2012).

It is possible that gestational changes in the microbiome may occur as a natural mechanism to prepare for the initial transfer of microbes to newborns. This transfer of microbes from mother to newborn may have implications on the transition of newborns to the extrauterine environment. Much more research, however, is needed to understand the physiologic role of microbes during gestation and its impact on nursing care practices for women and newborns.

Implications of Route of Birth

Vaginal birth remains the most common method of birth and is achieved by 68% of women in the United States (Martin, Hamilton, Osterman, Driscoll, & Mathews, 2017). The vaginal microbiome is a mutualistic environment of organisms that are dependent on environmental conditions and host factors that promote homeostasis in the vagina and inhibit growth of bacteria that have been associated with preterm labor and chorioamnionitis (Hyman et al., 2014). *Lactobacillus spp.* dominate the vaginal landscape and inhibit the growth of pathogenic bacteria by creating an acidic environment and competing for nutrients (Huang, Fettweis, Brooks, Jefferson, Buck, 2014). Additionally, periodic hormonal cycles and continual sloughing of epithelial cells contribute to the maintenance of healthy vaginal flora.

Vaginal bacterial communities differ by ethnic group. A study of 1290 women identified significantly different microbiome profiles between African American women and women of European ancestry (Huang, 2014). Specifically, African American women demonstrated a higher pH, greater variety of vaginal genus-level profiles dominated by anaerobic species, and smaller communities of protective species specifically *lactobacilli* (Huang, 2014). *Lactobacilli* produce an acidic vaginal environment, a protective factor for development of potentially harmful organisms in the vagina. A vaginal microbiome with a higher pH and

greater diversity of anaerobic species also contributes to a higher incidence of sexually transmitted infections and growth of other organisms associated with adverse pregnancy outcomes including preterm birth (Huang, 2014; Dunlop et al, 2015).

Children born via cesarean compared to those born vaginally are more likely to develop immune-related disorders like asthma/allergies (Black, Bhattacharya, Philip, Norman, & McLernon, 2016; Kristensen & Henriksen, 2016), inflammatory bowel disease (Kristensen & Henriksen, 2016), and obesity (Bernardi et al., 2015; Li, Zhou, & Liu, 2013; Mueller et al., 2015). Although not all of these associations are shown consistently in all studies (Bernstein et al., 2016; Black et al., 2016), these findings have led some researchers to speculate that alterations in microbiome seeding of newborns following cesarean birth may play some role in these associations between chronic disease and route of birth (Dominguez-Bello et al., 2016; Goedert, Hua, Yu, & Shi, 2014).

Adults born via cesarean birth have fecal microbiome/microbiota that are distinctly different than those of adults born vaginally (Goedert et al., 2014). Cesarean birth results in a gut microbiome that is less similar to that of the mother compared to vaginal birth (Backhed et al., 2015), and is more likely to include skin and oral microbes, and bacteria from the operating room (Backhed et al., 2015).

It appears that any contact between the unborn fetus and the mothers' vaginal microbiome (for example, through rupture of membranes in labor) results in early microbial seeding and potential long-term health benefits for the newborn. In a study of 18 maternal/newborn dyads, the microbiome of mothers and babies in three groups were compared: newborns born vaginally, newborns born via cesarean with standard post-op treatment, and newborns born via cesarean who were exposed to maternal vaginal fluids immediately following birth (Dominguez-Bello et al., 2016). Within two minutes of birth, newborns in the last group had their mouth, face, and body swabbed with a gauze pad that had been incubated for an hour in their mothers' vagina. These gut, oral, and skin microbiome of these newborns were more similar to vaginally-born newborns than to other newborns who experienced the standard cesarean birth. This similarity persisted through one month of life, when the study ended. These findings are consistent with population-based studies showing that children born via elective cesarean birth (no labor) are at higher risk for health problems like asthma compared to children who had some exposure to their mother's vaginal microbiome during labor, even if labor ended in cesarean (Kristensen & Henriksen, 2016).

Cesarean birth as currently practiced in most hospitals in the United States has additional implications on neonatal microbiome seeding. In conventional cesarean birth practices, newborns do not experience skin-to-skin with their mother until several hours following birth, during which time the newborn is handled by healthcare providers, receives a bath, and touches various operating room and recovery room surfaces. Family-centered cesarean birth, or skin-to-skin cesarean birth, is a new option that involves immediate skin-to-skin contact between the newborn and mother in surgery. However, this new cesarean protocol has not been widely adopted in hospitals due to safety concerns around the mother's ability to hold her newborn while on an operating room table and concerns related to postpartum hemorrhage and infection (Posthuma et al., 2016). In a recent study comparing conventional

cesarean birth to skin-to-skin cesarean birth, investigators did not see increases in either of these adverse outcomes, but did find that skin-to-skin treatment was associated with a decrease in both neonatal admission to the neonatal nursery and neonatal work-ups for infection (Posthuma et al., 2016).

Another implication of cesarean birth on neonatal microbiome seeding is early exposure to antibiotics in women having cesarean. Almost all women having cesarean birth receive intrapartum antibiotics to decrease their risk of post-operative infection (Smaill & Grivell, 2014). These powerful intravenous antibiotics are quickly transmitted to the fetus through the placenta, and are thus in active circulation in both mother and newborn at time of birth, with unknown implications on microbiota transfer.

Cesarean birth may also influence the neonatal microbiome seeding process via delayed breastfeeding initiation. Compared to newborns born vaginally, newborns born via cesarean are nearly half as likely to initiate breastfeeding before hospital discharge (Prior et al., 2012) and are more likely to have breastfeeding difficulties (Karlstrom, Lindgren, & Hildingsson, 2013). Thus, microbiota transmission via breastfeeding is delayed or eliminated in many cesarean-born babies. Antibiotics given to almost all women having cesarean birth lower the counts in breastmilk of *Bifidobacterium* species, which are known to prevent infection and provide anticarcinogenic capabilities to the newborn (Quigley, O'Sullivan, Stanton, et al 2013). Therefore, cesarean birth appears to decrease both the quantity and quality of human breastmilk, limiting an essential source of new microbial communities for the newborn.

Cesarean birth more often results in separation of the mother and newborn for several hours following birth with implications for neonatal microbiota seeding. Planned cesarean birth is associated with nearly twice the rate of newborn transfers to the neonatal intensive care unit and diagnosis of pulmonary disorders like transient tachypnea of the newborn as planned vaginal birth (Kolas, Saugstad, Daltveit, Nilsen, & Oian, 2006). Although typically these problems do not involve long-term nursery stays, this early exposure of newborns born via cesarean birth to nursery environments instead of maternal-focused environments potentially increases the influence of cesarean mode of birth on optimal early newborn microbiota formation.

Antibiotic Use during Labor and Implications

There is evidence that use of antibiotics prior to and during birth may disturb the activities of the host microbiome (Langdon, Crook, & Dantas, 2016). In non-pregnant populations, dysbiosis (imbalance) in the composition of the microbiome is associated with a range of metabolic and immunological complications as well as an increased susceptibility to infection (Langdon et al., 2016; Nuriel-Ohayon et al., 2016). A recent animal study found that use of select antibiotics (azithromycin, amoxicillin, cefaclor) increased the relative abundance of *Firmicutes*, a phylum of bacteria associated with fat absorption; additionally, mice demonstrated decreased overall species diversity with an additional side effect of weight gain (Khan et al., 2016). Antibiotic use during the intrapartum period has also been associated with lower levels of protective species bacteria including *Lactobacillus* and *Bifidobacteria* in the gut microbiome of newborns (Mshvildadze et al., 2010). Considering

that the first microbial exposure is likely to occur prior to birth, careful and parsimonious use of antibiotics prenatally is warranted as there may be additional effects on the microbiome of mothers and newborns.

Many women are prescribed antibiotics throughout pregnancy, several of which are known to cross the placenta and transfer to the fetus (Nahum, Uhl, & Kennedy, 2006). During labor, antibiotics are prescribed routinely to prevent complications from clinical issues such as Group B streptococcus colonization, chorioamnionitis, and prolonged preterm ruptured membranes, however the effects of prophylactic administration of antibiotics on the dynamics and structure of the maternal and newborn microbiome has been minimally considered. Use of intrapartum antibiotics has resulted in a drastic decrease in complications resulting from pathogen exposure, however the use of antibiotics on such a large scale has resulted in the emergence of drug resistant infectious pathogens such as methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile* in both mothers and newborns (Ledger, 2006). Antibiotic use during labor may also potentially increase the risk of infant gut dysbiosis, particularly among babies born preterm, as preterm infants are more likely to have abnormal colonization processes and increased risk for potential overgrowth of hospital acquired pathogens (Westerbeek et al., 2006). Although the use of antibiotics overall is associated with improved health outcomes, careful consideration should be given to the potential side effect on the maternal-newborn microbiome.

Clinical Implications of Nursing Care Procedures on the Microbiome

Several routine processes carried out by the nurse in the labor and birth environment have potential to influence the microbiome (See table 2). One of the primary tasks of the labor, birth, and recovery nurse is to ensure safe progression of labor which often includes cervical exams along with internal fetal heart rate and uterine contraction monitoring. While these tasks are fundamental, they still offer plenty of room to exercise prudent clinical judgment to minimize disturbance to the microbiome. One most obvious, but contentious, issue is unnecessary or excessive cervical examinations that can potentially introduce and facilitate infection (Cahill et al, 2012; Jackson, Morgan, Nichols, Shay, & Kim, 2010). Other tasks such as placing intrauterine pressure catheters, urinary catheters, and fetal scalp electrodes may also be seen as opportunities to introduce foreign bacteria (Harper, Shanks, Tuuli, Roehl, & Cahill, 2013; Wilson, Passante, Rauschenbach, Yang, & Wong, 2015). Current evidence does not uniformly support that cervical exams, internal monitoring (the fetal scalp electrode, intrauterine pressure catheter), or urinary catheterization independently result in harmful shifts in the microbiome. However, there are indications that these procedures can increase risk for cesarean sections and infections resulting in the use of antibiotics, which have the potential to alter the microbiome (Harper, Shanks, Tuuli, Roehl, & Cahill, 2013; Jansen, Gibson, Bowles, & Leach, 2013; Li, Wen, Wang, Li, & Li, 2011). As microbiome research expands we will learn more about how various procedures are related to shifts in the microbiome, and in turn, how it can influence the development of adverse health outcomes. Despite missing chains in the causal link, invasive procedures such as these should continue to be used judiciously and carried out in sterile conditions to reduce risk of infection (Jansen, Gibson, Bowles, & Leach, 2013).

Another key opportunity for labor nurses to preserve the maternal-newborn microbiome is to cultivate a labor environment that is supportive of vaginal birth by providing nursing care that is cognizant of the physiology of labor and nurturing to a woman's ever-changing needs throughout her labor process (Adams, Stark & Low, 2016). Nurses can increase the chance of vaginal birth by providing labor care that protects against unnecessary interventions including cesareans, such as by following newest evidence-based guidelines on normal labor progression and fetal heart rate surveillance in labor (American College of Obstetricians and Gynecologists [ACOG], 2017; ACOG & Society for Maternal-Fetal Medicine, 2014; Spong, Berghella, Wenstrom, Mercer, & Saade, 2012). When physically able, women should be encouraged to change positions throughout labor to facilitate the fetus's passage through the pelvis. Hydration and proper nutritional support should be maintained, as well as emotional support for the duration of the labor. Once the newborn arrives, the labor nurse is uniquely positioned to promote the new mother or partner to maintain skin to skin contact for immediate newborn assessment, such as Apgar scoring, and prompt initiation of breastfeeding if desired. Skin-to-skin contact and breastfeeding help to further seed the newborn with maternal microbes (Rautava, Luoto, Salminen, & Isolauri, 2012).

Conclusion

Patient education about prenatal influences on the microbiome, birth route factors, antibiotic use during pregnancy and labor, and nursing care that support vaginal birth are the major avenues through which nurses in labor and birth units have opportunities to influence the microbial environment of both the mother and newborn. Although the relationships between the microbiome and health outcomes are not yet fully understood, nurses are uniquely positioned to provide evidence-based supportive care during labor, birth, and postpartum as well as provide education to mothers and their families about the adoption of health behaviors that may potentially promote healthy initial interactions between the maternal-child microbiome. Several nursing care procedures that conserve the microbiome are already followed and should be further promoted including protecting the first hour after birth for uninterrupted skin-to-skin care and initiation of breastfeeding (Crenshaw, 2014). As research clarifies the relationships between the microbiome and the relationship to maternal-child health outcomes, further recommendations can be made to advance practice for women and their newborns.

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Callouts

- “Seeding” or the transfer of microbes from mother to newborn is influenced by a variety of factors related to the labor and birth process.
- The intrauterine environment, although traditionally considered to be sterile and free of microbes, has been found to harbor a variety of microbes.
- Newborns born via cesarean tend to have a gut microbiome less similar to that of their mother compared to those born vaginally; microbes are more likely to include skin and oral microbiota as well as bacteria from operating room environments.
- It is hypothesized that delayed initiation of breastfeeding may alter and potentially have a negative influence on the initial seeding process of the neonatal microbiome.
- Antibiotic use during the intrapartum period has been associated with lower levels of protective bacterial species in newborns as well as the emergence of drug resistant pathogens in mothers and newborns, however the long-term effects on the microbiome are not fully known.

Clinical Implications

- Protecting the integrity of the maternal-newborn microbiome requires that nurses follow evidence based guidelines for supporting vaginal birth, breastfeeding initiation, and skin-to-skin care.
- Infection control procedures are imperative to avoid unnecessary exposure to foreign and/or harmful bacteria.
- Patient education about the potential effects of antibiotics on the structure and function of the maternal-infant microbiome may become important as more is discovered about the relationship between the microbiome and health.
- Harmful shifts in the maternal-newborn microbiome can increase risk for both short and long term adverse health outcomes.

Table 1

Definitions of Commonly Used Terms

Human microbiome: the collective genomes of the microbiota (composed of bacteria, bacteriophage, fungi, protozoa and viruses) that live inside and on the human body

Genomes: the complete set of genetic material present in a cell or organism.

Microbiota: the community of commensal, symbiotic and pathogenic microorganisms that share our body space

Species diversity: the number of species present and the abundance of each within a select body site

Table 2

Nursing Care Procedures that have the Potential to Influence the Microbiome

•	Cervical Exams
•	Intrauterine Fetal Heart Rate (fetal scalp electrode)
•	Uterine Contraction Monitoring (intrauterine pressure catheter)
•	Urinary Catheterization
•	Antibiotic Administration
•	Breastfeeding Initiation
•	Promotion of Uninterrupted Skin to Skin Interactions
