Gynecology and Obstetrics Clinical Medicine 1 (2021) 79–82

Contents lists available at ScienceDirect

Gynecology and Obstetrics Clinical Medicine

journal homepage: www.keaipublishing.com/en/journals/gynecology-and-obstetrics-clinical-medicine

Early-life gut microbiota development from maternal vertical transmission

Jing Wang, Li Lin *

Department of Obstetrics and Gynecology, Peking University International Hospital, 1 Life Park Road, Life Science Park of Zhong Guancun, Changping District, Beijing, 102206, PR China

A B S T R A C T

The gut microbiota of early life is crucial for childhood growth and development. Maternal gut microbiota directly or indirectly affects the colonization and development of early-life gut microbiota. Factors such as delivery mode, feeding mode, gestational age at birth, diet, and antibiotic use, can influence the vertical transmission of maternal gut microbiota to infants and affect the development of metabolic, endocrine, neural, and immune pathways in the early life. In this review, we summarize the latest knowledge of factors affecting early-life gut microbiota from maternal vertical transmission.

In recent years, authors of emerging studies have found that changes in maternal microecological community, particularly those of gut microbiota, are closely related to complications in pregnancy and could affect the colonization and development of early-life gut microbiome. The first 1000 days – that is, the period from conception to two years of age – is critical for early childhood growth and development. This paper includes a review of the factors influencing the vertical transmission of maternal gut microbiota to the colonization and development of early-life gut microbiota.

1. Gut microbiota

Human microorganisms tend to be distributed in the intestine, mouth, respiratory tract, urogenital tract, and skin, most of which are colonized in the intestine. There are many gut microorganisms that inhabit more than 100 trillion microorganisms. These mainly include bacteria, archaea, fungi, and viruses, of which more than 99% are bacteria.[1] Humans have symbiotically co-evolved with these microorganisms. More than 99% of bacteria belong to five major phyla[2]: *Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria,* and *Verrucomicrobia.*

The gut microbial community is both complex and diverse, as is essential for maintaining the physiological dynamic balance of the human body. Its genome is known as the 'second genome' of human beings.[3] The gut microbiome is closely related to human metabolism and can regulate the expression of approximately 10% of host transcription genes, especially those related to cell proliferation, immunity, and metabolism.[4] Gut microbiota can regulate the absorption of food energy, as well as decomposing lactic acid, hydrogen sulfide, and other toxic and harmful substances in the human body. It can also provide various essential amino acids and vitamins, as well as some antibiotics and peptides for the human body, and can regulate host gene expression, intestinal peptide hormone secretion, choline, and bile acid metabolism, and other mechanisms for maintaining the body's stability. Rastelli et al.[5] suggested that gut microbiota was an important endocrine organ that could communicate with human organs in a variety of ways, such as by stimulating key receptors or specific hormones through nutrients or metabolites (for example, 5-hydroxytryptamine), and produce regulatory effects. Authors of recent studies have found that the metabolites of gut microbiota play a vital role in organs other than the gastrointestinal tract, through the gut-brain axis, gut-liver axis, gut-kidney axis, gut-lung axis, and gut-heart axis.[6] Gut microbiome dysbiosis could lead to a variety of diseases including kidney diseases, hypertension, diabetes mellitus, obesity, lipid metabolism disorders, and so on. Additionally, disordered gut microbiota is related to cystic fibrosis, inflammatory bowel disease, colon cancer, nervous system diseases (including Alzheimer's disease, Parkinson's disease, and multiple sclerosis), musculoskeletal and autoimmune diseases (including rheumatoid arthritis, systemic lupus erythematosus, and so on) as well as other diseases.[7]

* Corresponding author.
E-mail address: linli488@aliyun.com (L. Lin).

Publishing services by Elsevier on behalf of KeAi

https://doi.org/10.1016/j.gocm.2021.03.008
Received 20 December 2020; Received in revised form 14 March 2021; Accepted 30 March 2021
Available online 25 April 2021

2. Maternal gut microbiota during pregnancy

Many physiological changes to glucose and lipid metabolism might occur during pregnancy. Throughout a typical, healthy pregnancy, women experience immunological, hormonal, and metabolic changes. To ensure sufficient energy intake for the nutritional needs of both fetal and the women's own development, the body will increase fat and decrease insulin sensitivity, both of which are related to the self-regulation of the gut microbiome in pregnant women. Koren et al.[8] suggested that during early pregnancy, numbers of butyrate-producing bacteria, such as *Faecalibacterium* and *Eubacterium*, increased, while butyrate, which has anti-inflammatory and immune regulation functions, could prevent maternal immune responses toward the fetal allograft. Such changes may be related to maternal endocrine and immune regulation to adapt to pregnancy. From early to late pregnancy, gut microbiota diversity decreased, while *Proteobacteria* and *Actinobacteria* increased. During late pregnancy, the α diversity of gut microbiota decreased while the β diversity of gut microbiota increased. Additionally, the increase of *Lactobacillus* species related to lactic acid fermentation in the intestinal tract may be related to gut microbiota colonization in the infants as well as the digestion and absorption of lactose in mother's milk.

3. Early-life gut microbiota

An infant's gut microbiota typically includes four phyla; that is, *Actinobacteria, Proteobacteria, Firmicutes,* and *Bacteroidetes*.[9] A key source of infant gut microbiota is the mother; microbiota can be transmitted vertically from the maternal gut microbiota, vaginal microbiota, and breast milk. In a cohort of 25 Italian infants, it was found that more than half of the bacterial species in the infants' gut originated from the guts, vaginas, mouths, and skin of their mothers.[10]

The construction of healthy newborns' gut microbiota tends to be derived from maternal gut microbial community. Additionally, the establishment of gut microbiota during early life is a continuous process, beginning in the uterus and continuing until two to three years after birth. This is important for the development of immune and digestive systems in both infants and young children.[11]

Whether the placenta is sterile remains controversial.[12,13] Many authors cite the existence of microbiota in human placental tissues and amniotic fluid, supporting the mother-to-infant microbiota transmission. Theis et al.[14] used electron microscopy to find granular and bacteria-like structures in the intestinal tract of the fetus. Combined with culture omics, these were regarded as a type of active bacteria with low abundance which impacted the intestinal development and immunity of newborns. Thus, it was found that newborns interacted with microorganisms before birth. Dong et al.[15] carried out a paired study and found a similar microbial composition in the placenta, amniotic fluid, and neonatal feces.

Following birth, facultative bacteria and aerotolerant microorganisms such as *Proteobacteria* appear immediately, leading to oxygen depletion in the gut and subsequent colonization by strict anaerobes.[9] Authors of a recent study found that, by day seven after birth, the microbiota of vaginal-born infants was mainly facultative anaerobic bacteria; that is, *Bifidobacterium, Escherichia, Bacteroides,* and *Parabacteroides*.[16]

Weaning and intake of solid food are important for the development of an infant's gut microbiota. In a longitudinal study of 43 US infants from birth to 2–3 years, solid food intake resulted in a decrease of *Bifidobacterium, Bacteroides,* and *Clostridium*, and an increase in a diverse mixture of *Clostridiales* from six to 24 months after birth.[17] With age, alpha diversity increases, in particular between one and two years after birth.[18] The infant gut microbiota from birth to two years old is affected by many factors. The microbiome could be targeted to optimize healthy composition with successful interventions in this period. However, after two years, the gut microbiota is almost fixed and stabilized, as it is in adults.[19] This means that different unique gut microbiota and microbiota-targeted interventions during this period may be less effective for growth.[20]

There is emerging evidence to suggest that the colonization of microbes during early life is critical for early childhood growth and development. Authors of numerous studies have found that infant gut microbiota plays a key role in allergies such as atopic eczema and asthma, obesity and obesity-related disorders, and other chronic disorders such as irritable bowel syndrome, and type 1 diabetes mellitus, and so on.[20]

The establishment, development, and maturation of gut microbiota in early life are affected by many factors, such as delivery mode, feeding mode, gestational age, complications in pregnancy, diet, antibiotics, and so on.[9]

3.1. Delivery mode

Researchers have found that, during the first few weeks after birth, delivery mode is a major determinant of gut microbiota.[21] Differences in infants' microbiota as a result of birth mode have been observed. Many more strains are transmitted to vaginal-born babies than those delivered by cesarean section. Strains of *Bacteroides* and *Actinomycetes* (especially *Bacteroides* and *Bifidobacterium*) are only passed on during vaginal delivery. The gut microbiota of 98 Swedish mothers was analyzed days after delivery, while those of their full-term infants were analyzed in the first week after birth as well as at four and 12 months of age. The researchers observed a 72% correspondence in meta OTUs in mother-newborn pairs following vaginal delivery, compared to 41% after cesarean-section, indicating vertical transmission. The guts of naturally delivered newborns are initially colonized by relatively aerobic bacteria (*Enterococcus*, *Escherichia/Shigella*, *Streptococcus,* and *Rothia*), as well as by the anaerobic bacteria (*Bifidobacterium, Lactobacillus, Collinsella, Granulicatella*, and *Veillonella*) which is involved in lactate metabolism during lactation, fiber and carbohydrate degradation, and SCFAs (short chain fatty acids) production, resembling maternal microbiota.[21]

The gut microbiota of infants born vaginally is closer to maternal vaginal microbiota and is composed of *Bifidobacterium, Escherichia*, *Bacteroides,* and *Parabacteroides*. In contrast, that of cesarean-section infants is unstable, more like the external environment (since the first major microorganism to be exposed by cesarean section infants is the mother's skin and/or the surrounding environment of major genera including *Enterococcus, Enterobacter,* and *Klebsiella* species), more likely to carry potential pathogens, and easier to change.[16]

In October 2020, a study into fecal microbiota transplantation of maternal diluted feces mixed with colostrum in cesarean-born infants was conducted.[22] It was found that the microbial composition of these infants at three months was closer to that of natural delivery infants and differed significantly from other infants born by cesarean-section who did not receive their mothers' feces. It is, therefore, suggested that newborn microbiome after cesarean-section can be remodeled by fecal transplantation.[22]

3.2. Feeding mode

Human breastmilk contains 10^2-10^4 viable bacteria per mL, which directly affects the neonatal microbiota establishment. Additionally, *Lactobacillus, Staphylococcus, Enterococcus,* and *Bifidobacterium* can be transferred via lactation.[23] Differences in gut microbiota between breastfeeding and formula feeding are large, greatly impacting newborns' immunity.[24] The source of bacteria in breast milk remains controversial. Some believe that human milk bacteria are derived from the mother's skin, as there are some common bacteria in human milk.[25] However, most authors suggest that the transport of bacteria from the mother's gut to the mammary gland is the main pathway.[25] Breast-fed newborns may have more beneficial bacterial strains, such as *Bifidobacteria* and *Lactobacillus*, while proportions of potentially pathogenic bacteria such as *Clostridium* are lower. Compared with formula-fed children, the absolute concentration of SCFAs in the feces of breast-fed infants was lower. This may be due to lower microbial diversity and higher lactic acid concentration. However, there was a higher proportion of acetate in breast-fed children.[26]

Antimicrobial factors in breast milk may affect microbiota. Breast milk is the primary source of lactoferrin in infants, protecting against bacterial invasion by isolating iron from bacterial pathogens as well as interacting directly with bacteria.[27] The development of beneficial microbiota relies on the ability to protect infants from pathogenic microorganisms.[27]

3.3. Full-term and premature infants

In vaginally term-born infants, facultative anaerobic microbiota such as *Proteobacteria* are gradually replaced by anaerobes such as *Bifidobacterium* and *Clostridium*.[28] Compared to full-term infants, preterm infants have less bacterial diversity and more potential pathogens. They tend to have a high abundance of *Enterobacteriaceae, Staphylococcaceae,* and *Enterococcaceae* as well as low and delayed colonization of *Bifidobacterium*.[29]

Gilson et al.[30] found that six bacteria species (*Enterococcus faecalis, Enterobacter cloacae, Staphylococcus epidermidis, Escherichia coli, Klebsiella pneumoniae,* and *Klebsiella oxytoca*) were abundant in preterm infants' gut microbiota, increases in proportions of potential pathogens including *Clostridium difficile* and *Klebsiella pneumoniae* have been observed in preterm infants. Additionally, compared to full-term, preterm infants had fewer bacterial species, with reduced *Bifidobacterium, Bacteroides,* and *Atopobium*, as well as increased facultative anaerobes, which may delay immune system maturation in these infants.[31]

Milk feeding helps efficient digestion and absorption of nutrients by structural and functional maturation of the gastrointestinal tract.[27] During preterm births, infants suffered from immature digestion and motility. Lactase activity, which is key for milk lactose degradation, increases progressively from 24 to 40 weeks of gestation.[32] An immature gastrointestinal barrier and nutrient absorption affect the abnormal colonization of gut microbiota in preterm infants.

3.4. Complications in pregnancy

Significantly altered gut microbiota has been found in pregnant women with gestational diabetes mellitus (GDM), gestational hypertension, and other metabolic diseases during pregnancy. Kuang et al.[33] found that, compared with healthy pregnant women, *Parabacteroides distasonis, Klebsiella variicola*, and so on were enriched in GDM patients, while *Methanobrevibacter smithii, Alistipes* spp., *Bifidobacterium* spp., and *Eubacterium* spp. were enriched in the control group. Wang et al.[34] found consistent changes in the microbiota of GDM pregnant women and their newborns in multiple specimens. The metabolic capacity of neonatal intestinal bacteria in pregnant women with GDM decreased. These crucial breakthroughs emphasize the key role of healthy gut microbiota in shaping newborns' initial gut microbiome. The discovery of some high abundance bacteria related to GDM as well as oral glucose tolerance tests may provide markers for clinical testing of GDM. It is suggested that maternal gut microbiota dysbiosis may affect the gut microbiome of newborns.

Additionally, women who are obese before pregnancy and/or during pregnancy as well as excessive gestational weight gain (GWG) are associated with maternal gut microbiota dysbiosis, such as a higher abundance of *Bacteroides, Clostridium,* and *Staphylococcus*.[35] Furthermore, GWG is strongly associated with the metabolic pathways of the infant microbiota for the first eight months, indicating that GWG may influence specific gut microbiota transmission into infants.[36]

3.5. Maternal diet

The maternal microbiota which is altered by diet could affect transmission to the offspring. In one cohort, based on a dietary questionnaire, infants born to a maternal high-fat (>40%) gestational diet had enriched *Lactococcus, Enterococcus,* and *Granulicatella*, and a decrease of *Bacteroides, Parabacteroides, Sutterella,* and *Comamonas*. This influence could persist to six weeks of age.[37]

It has also been found that a higher maternal intake of saturated fatty acids (SFA) is significantly associated with higher *Firmicutes* and lower *Proteobacteria*, while higher maternal intakes of fiber and vegetable protein are associated with lower *Bacteroidetes* in neonatal gut microbiota.[38] In a nested cross-sectional study with the longitudinal MAMI cohort, it was found that the existing association between maternal diet, intestinal producers, and neonatal gut microbiota is mostly influenced by the intake of SFA and monounsaturated fatty acids. Members of *Firmicutes* in the neonatal microbiota were positively associated with maternal fat intake and negatively correlated to fiber, vegetable proteins, and vitamins.[39]

Maternal diet may be an important factor for modulating a mother's colostrum HMO (Human milk oligosaccharides) levels. A large, double-blind, placebo-controlled randomized clinical trial of probiotic supplementation study was carried out with 1223 pregnant mothers from Finland.[40] It was found that concentrations of HMO such as 3-fucosyllactose and 3′-sialyllactose were significantly higher in colostrum from the mothers in the probiotic supplementation group compared to those in the non-supplemented group. HMO is a major substrate for infants' gut microbiota which affects the maturation of the intestinal mucosal immune system. Maternal probiotic supplementation during the third trimester of pregnancy may change HMO composition in human milk, thus affecting infants' gut microbiota.[40]

3.6. Antibiotics

Neonatal gut microbiota is influenced by maternally administered antibiotics. These antibiotics have a prophylactic use during childbirth, following guidelines, or non-prophylactic use during pregnancy and before delivery. Zimmermann et al.[41] conducted a study on 272 infants and found that, compared to non-exposed infants, infants who were exposed to GBS (group B streptococcus) IAP (intrapartum antibiotic prophylaxis) had a lower bacterial diversity, a lower relative abundance of *Actinobacteria*, especially *Bifidobacteriaceae*, and a larger relative abundance of *Proteobacteria* in their gut microbiota. Antibiotics may reduce the stability, diversity, and richness of intestinal microbiota in infants, with increased *Proteobacteria*, including *Enterobacteriaceae* and drug resistance genes,[42] decreased proportions in *Actinobacteria, Firmicutes,* and *Bacteriodetes* as well as decreased diversity.[43]

Antibiotics may affect the early colonization of microorganisms in several ways. Firstly, antibiotics administered maternally reach newborns' blood stream through the umbilical cord and remain in place for at least 10 h following administration. They may also affect early colonization of gut microbiota.[44] Secondly, antibiotics administered maternally can change mothers' vaginal and gut microbiota, thus affecting the vertical microbial transmission process.[45] Thirdly, antibiotic therapy independently affects the composition of breast milk microbiota following delivery.[46]

In conclusion, maternal gut microbiota directly or indirectly affects the colonization and development of early-life gut microbiota. Factors including delivery and feeding mode, gestational age at birth, diet, and antibiotic use can influence the maternal vertical transmission of gut microbiota to infants as well as affecting the development of metabolic, endocrine, neural, and immune pathways in early life. Thus, in the future, systematic and prospective research should be carried out to investigate maternal and infant gut microbiota, providing opportunities to improve maternal and infant health.

Funding

This work was supported by Peking University International Hospital Research Funds (No.YN2020QN02).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Ley RE, Peterson DA, Gordon JI. Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell*. 2006;124:837–848. https://doi.org/10.1016/j.cell.2006.02.017.
2. Sender R, Fuchs S, Milo R. Are we really vastly outnumbered? Revisiting the ratio of bacterial to host cells in humans. *Cell*. 2016;164:337–340. https://doi.org/10.1016/j.cell.2016.01.013.
3. Relman DA, Falkow S. The meaning and impact of the human genome sequence for microbiology. *Trends Microbiol*. 2001;9:206–208. https://doi.org/10.1016/s0966-842x(01)02041-8.
4. Sommer F, Nookaew I, Sommer N, et al. Site-specific programming of the host epithelial transcriptome by the gut microbiota. *Genome Biol*. 2015;16:62. https://doi.org/10.1186/s13059-015-0614-4.
5. Rastelli M, Cani PD, Knauf C. The gut microbiome influences host endocrine functions. *Endocr Rev*. 2019;40:1271–1284. https://doi.org/10.1210/er.2018-00280.
6. Ver Heul A, Planer J, Kau AL. The human microbiota and asthma. *Clin Rev Allergy Immunol*. 2019;57:350–363. https://doi.org/10.1007/s12016-018-8719-7.
7. Buford TW. (Dis)Trust your gut: the gut microbiome in age-related inflammation, health, and disease. *Microbiome*. 2017;5:80. https://doi.org/10.1186/s40168-017-0296-0.
8. Koren O, Goodrich JK, Cullender TC, et al. Host remodeling of the gut microbiome and metabolic changes during pregnancy. *Cell*. 2012;150:470–480. https://doi.org/10.1016/j.cell.2012.07.008.
9. Dogra S, Sakwinska O, Soh SE, et al. Dynamics of infant gut microbiota are influenced by delivery mode and gestational duration and are associated with subsequent adiposity. *mBio*. 2015;6. https://doi.org/10.1128/mBio.02419-14.
10. Ferretti P, Pasolli E, Tett A, et al. Mother-to-Infant microbial transmission from different body sites shapes the developing infant gut microbiome. *Cell Host Microbe*. 2018;24:133–145. https://doi.org/10.1016/j.chom.2018.06.005. e135.
11. Davis KL. Low gut microbiota diversity in early infancy precedes asthma at school age. *Pediatrics*. 2015;136:S232. https://doi.org/10.1542/peds.2015-2776T. S232.
12. Blaser MJ, Dominguez-Bello MG. The human microbiome before birth. *Cell Host Microbe*. 2016;20:558–560. https://doi.org/10.1016/j.chom.2016.10.014.
13. Hornef M, Penders J. Does a prenatal bacterial microbiota exist? *Mucosal Immunol*. 2017;10:598–601. https://doi.org/10.1038/mi.2016.141.
14. Theis KR, Romero R, Winters AD, et al. Does the human placenta delivered at term have a microbiota? Results of cultivation, quantitative real-time PCR, 16S rRNA gene sequencing, and metagenomics. *Am J Obstet Gynecol*. 2019;220:267. https://doi.org/10.1016/j.ajog.2018.10.018. e261-267.e239.
15. Dong XD, Li XR, Luan JJ, et al. Bacterial communities in neonatal feces are similar to mothers' placentae. *Can J Infect Dis Med Microbiol*. 2015;26:90–94. https://doi.org/10.1155/2015/737294.
16. Shao Y, Forster SC, Tsaliki E, et al. Stunted microbiota and opportunistic pathogen colonization in caesarean-section birth. *Nature*. 2019;574:117–121. https://doi.org/10.1038/s41586-019-1560-1.
17. Bokulich NA, Chung J, Battaglia T, et al. Antibiotics, birth mode, and diet shape microbiome maturation during early life. *Sci Transl Med*. 2016;8. https://doi.org/10.1126/scitranslmed.aad7121, 343ra382.
18. Fouhy F, Watkins C, Hill CJ, et al. Perinatal factors affect the gut microbiota up to four years after birth. *Nat Commun*. 2019;10:1517. https://doi.org/10.1038/s41467-019-09252-4.
19. Yatsunenko T, Rey FE, Manary MJ, et al. Human gut microbiome viewed across age and geography. *Nature*. 2012;486:222–227. https://doi.org/10.1038/nature11053.
20. Robertson RC, Manges AR, Finlay BB, et al. The human microbiome and child growth - first 1000 Days and beyond. *Trends Microbiol*. 2019;27(2):131–147. https://doi.org/10.1016/j.tim.2018.09.008.
21. Bäckhed F, Roswall J, Peng Y, et al. Dynamics and stabilization of the human gut microbiome during the first year of life. *Cell Host Microbe*. 2015;17:690–703. https://doi.org/10.1016/j.chom.2015.04.004.
22. Korpela K, Helve O, Kolho KL, et al. Maternal fecal microbiota transplantation in cesarean-born infants rapidly restores normal gut microbial development: a proof-of-concept study. *Cell*. 2020;183:324–334. https://doi.org/10.1016/j.cell.2020.08.047. e325.
23. Fernández L, Langa S, Martín V, et al. The human milk microbiota: origin and potential roles in health and disease. *Pharmacol Res*. 2013;69:1–10. https://doi.org/10.1016/j.phrs.2012.09.001.
24. Janzon A, Goodrich JK, Koren O, et al. Interactions between the gut microbiome and mucosal immunoglobulins A, M, and G in the developing infant gut. *mSystems*. 2019;4. https://doi.org/10.1128/mSystems.00612-19.
25. Rautava S. Early microbial contact, the breast milk microbiome and child health. *J Dev Orig Health Dis*. 2016;7:5–14. https://doi.org/10.1017/s2040174415001233.
26. Bridgman SL, Azad MB, Field CJ, et al. Fecal short-chain fatty acid variations by breastfeeding status in infants at 4 Months: differences in relative versus absolute concentrations. *Front Nutr*. 2017;4:11. https://doi.org/10.3389/fnut.2017.00011.
27. Demmelmair H, Prell C, Timby N, et al. Benefits of lactoferrin, osteopontin and milk fat globule membranes for infants. *Nutrients*. 2017;9. https://doi.org/10.3390/nu9080817.
28. Korpela K, de Vos WM. Early life colonization of the human gut: microbes matter everywhere. *Curr Opin Microbiol*. 2018;44:70–78. https://doi.org/10.1016/j.mib.2018.06.003.
29. Patel AL, Mutlu EA, Sun Y, et al. Longitudinal survey of microbiota in hospitalized preterm very-low-birth-weight infants. *J Pediatr Gastroenterol Nutr*. 2016;62:292–303. https://doi.org/10.1097/mpg.0000000000000913.
30. Gibson MK, Wang B, Ahmadi S, et al. Developmental dynamics of the preterm infant gut microbiota and antibiotic resistome. *Nat Microbiol*. 2016;1:16024. https://doi.org/10.1038/nmicrobiol.2016.24.
31. Arboleya S, Binetti A, Salazar N, et al. Establishment and development of intestinal microbiota in preterm neonates. *FEMS Microbiol Ecol*. 2012;79:763–772. https://doi.org/10.1111/j.1574-6941.2011.01261.x.
32. Commare CE, Tappenden KA. Development of the infant intestine: implications for nutrition support. *Nutr Clin Pract*. 2007;22:159–173. https://doi.org/10.1177/0115426507022002159.
33. Kuang YS, Lu JH, Li SH, et al. Connections between the human gut microbiome and gestational diabetes mellitus. *GigaScience*. 2017;6:1–12. https://doi.org/10.1093/gigascience/gix058.
34. Wang J, Zheng J, Shi W, et al. Dysbiosis of maternal and neonatal microbiota associated with gestational diabetes mellitus. *Gut*. 2018;67:1614–1625. https://doi.org/10.1136/gutjnl-2018-315988.
35. Singh S, Karagas MR, Mueller NT. Charting the maternal and infant microbiome: what is the role of diabetes and obesity in pregnancy? *Curr Diabetes Rep*. 2017;17:11. https://doi.org/10.1007/s11892-017-0836-9.
36. Baumann-Dudenhoeffer AM, D'Souza AW, Tarr PI, et al. Infant diet and maternal gestational weight gain predict early metabolic maturation of gut microbiomes. *Nat Med*. 2018;24:1822–1829. https://doi.org/10.1038/s41591-018-0216-2.
37. Chu DM, Antony KM, Ma J, et al. The early infant gut microbiome varies in association with a maternal high-fat diet. *Genome Med*. 2016;8:77. https://doi.org/10.1186/s13073-016-0330-z.
38. Lundgren SN, Madan JC, Emond JA, et al. Maternal diet during pregnancy is related with the infant stool microbiome in a delivery mode-dependent manner. *Microbiome*. 2018;6:109. https://doi.org/10.1186/s40168-018-0490-8.
39. Selma-Royo M, García-Mantrana I, Calatayud M, et al. Maternal diet during pregnancy and intestinal markers are associated with early gut microbiota. *Eur J Nutr*. 2020. https://doi.org/10.1007/s00394-020-02337-7.
40. Seppo AE, Kukkonen AK, Kuitunen M, et al. Association of maternal probiotic supplementation with human milk oligosaccharide composition. *JAMA Pediatr*. 2019;173:286–288. https://doi.org/10.1001/jamapediatrics.2018.4835.
41. Zimmermann P, Curtis N. Effect of intrapartum antibiotics on the intestinal microbiota of infants: a systematic review. *Arch Dis Child Fetal Neonatal Ed*. 2020;105:201–208. https://doi.org/10.1136/archdischild-2018-316659.
42. Neuman H, Forsythe P, Uzan A, et al. Antibiotics in early life: dysbiosis and the damage done. *FEMS Microbiol Rev*. 2018;42:489–499. https://doi.org/10.1093/femsre/fuy018.
43. Lange K, Buerger M, Stallmach A, et al. Effects of antibiotics on gut microbiota. *Dig Dis*. 2016;34:260–268. https://doi.org/10.1159/000443360.
44. Pacifici GM. Placental transfer of antibiotics administered to the mother: a review. *Int J Clin Pharmacol Ther*. 2006;44:57–63. https://doi.org/10.5414/cpp44057.
45. Gomez de Agüero M, Ganal-Vonarburg SC, Fuhrer T, et al. The maternal microbiota drives early postnatal innate immune development. *Science*. 2016;351:1296–1302. https://doi.org/10.1126/science.aad2571.
46. Asbury MR, Butcher J, Copeland JK, et al. Mothers of preterm infants have individualized breast milk microbiota that changes temporally based on maternal characteristics. *Cell Host Microbe*. 2020;28:669–682. https://doi.org/10.1016/j.chom.2020.08.001. e664.