

Gorczyca, Kamila, Obuchowska, Aleksandra, Standyło, Arkadiusz, Obuchowska, Karolina, Kołodziej, Magdalena. The influence of nutrition on the development of the child's intestinal microflora. *Journal of Education, Health and Sport*. 2022;12(9):558-571. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2022.12.09.066>
<https://apcz.umk.pl/JEHS/article/view/39662>
<https://zenodo.org/record/7058464>

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343.

Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).

Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159.

Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

© The Authors 2022;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 21.08.2022. Revised: 02.09.2022. Accepted: 07.09.2022.

The influence of nutrition on the development of the child's intestinal microflora

Kamila Gorczyca¹, Aleksandra Obuchowska^{1*}, Arkadiusz Standyło^{1*},
Karolina Obuchowska¹, Magdalena Kołodziej

¹Student's Scientific Association at the Department of Obstetrics and Perinatology, Medical University of Lublin, 20-090 Lublin, Poland

*Correspondence Authors

Abstract: The intestinal microbiota, also known as the intestinal microflora, or the intestinal flora, is a group of microorganisms (microbiome), mainly bacteria, which form a complex ecosystem in the digestive system. In humans, it is one of the elements of his physiological biota [1].

Childbirth is an important stage in the colonization of the human digestive system by the microbiota. The form of feeding also plays an important role in the colonization of the intestines of a newborn and infant [2]. Breast milk has many benefits. Breastfeeding plays an important role in shaping baby's gut microbiota. Mother's milk contains health-promoting bacteria that support the primary colonization of the newborn's intestines. Diet has a significant influence on the formation of the intestinal microbiota. Therefore, it is important that a woman not only during the entire pregnancy, but also before pregnancy, takes care of a varied, balanced and rich in prebiotics diet [3].

Keywords: microbiota of a pregnant woman, diet, breastfeeding, childbirth.

1. Introduction

The gut microbiota is a group of microorganisms (microbiome), mainly bacteria, that form a complex ecosystem in the digestive system [4]. The intestinal biota bacteria are found mainly in the large intestine and are the basic mass of the stool [5]. The intestines contain 1,000 species of bacteria and 100 times more genes than the human genome [6]. The intestinal microbiota also includes fungi and protozoa [7].

In newborns, the digestive system is sterile, but it is later colonized by bacterial biota [8]. With aging, the total number of microorganisms does not change significantly, but there is usually a significant change in the share of particular groups. You can observe an increase in the number of enterobacteria, Clostridium and enterococci and a simultaneous decrease in the number of Lactobacillus and Bifidobacterium, which are considered beneficial to health [9].

The composition of the gut microbiota changes under the influence of a number of different factors [11], e.g.

1. food
2. hormones
3. the environment,
4. the type of delivery - whether by natural means or by caesarean section,
5. taking antibiotics and medications,
6. century
7. stress
8. diseases.

In recent years, there has been a significant increase in interest in the role of the intestinal microbiota in shaping human health and in the occurrence of intestinal dysbiosis in various disease entities, including Parkinson's disease, breast cancer, acute myeloid leukemia [12–14]. The intestinal microbiota is not only involved in the processes related to digestion and absorption of nutrients [15]. The bacteria that are part of the intestinal microbiota perform various important functions, and their correct quantitative and qualitative structure, the so-called eubiosis state, supports the homeostasis of the whole organism, thus shaping immunity, metabolism and the

synthesis of many chemical compounds, for example serotonin and neurotransmitter precursors [16–18].

The intestinal microbiota, also known as the intestinal microflora, or the intestinal flora, is a group of microorganisms (microbiome), mainly bacteria, which form a complex ecosystem in the digestive system. In humans, it is one of the elements of his physiological biota [19,20].

The relationship between the host and the bacterial biota on commensalism is a kind of favorable symbiosis [21]. Microorganisms perform many useful functions, such as:

1. fermentation of certain nutrients,
1. stimulation of the immune system in the fight against pathogenic microorganisms,
2. regulation of intestinal development,
3. production of vitamins (biotin and vitamin K),
4. hormone production.

Under certain conditions, certain species of the gut microbiota can cause disease states (opportunistic infections) or contribute to carcinogenesis. The gastrointestinal microbiome, which is regulated by the composition of the diet and nutritional status, also significantly affects the maintenance of the proper functioning of the brain [17,22].

Scientific research shows that the gut bacteria of a pregnant woman, her diet and health status have a significant and direct impact on the future profile of the baby's gut bacteria [3,23]. During pregnancy, the female body undergoes hormonal, metabolic, and immunological changes to preserve the health of both the mother and the offspring [24]. These changes alter the mother microbiota at different sites such as the gut, the vagina, and the oral cavity [25]. A number of factors might influence the microbiota profile such as the diet, antibiotic, or other supplement intakes, as well as the methodology of research [4,24,26].

2. Materials and Methods

Systematic searches were conducted in August 2022 using electronic databases such as Pubmed, Science Direct and Google Scholar in accordance with PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman and Group, 2009). The databases were checked by two independent authors. The following items were searched: (microbiota or microbiome) AND pregnancy; intestinal microflora and child development; microbiota and child nutrition. The articles you downloaded were first selected based on title and abstract. As a result, we identified a total of 235 articles related to the topic of interest to us. After considering the inclusion / exclusion criteria and eliminating duplicates, 32 studies were selected for analysis.

Inclusion criteria for selecting the study:

- the samples have been taken from the stool or placenta,
- randomized clinical trials, systemic reviews, meta-analyzes,
- Human Research.

Exclusion criteria:

- case reports, conference summaries, comments,
- insufficient amount of data,
- full-text article not available for review,
- a language other than English,
- non-human studies.

Key review references were hand searched to identify any relevant references that were omitted.

2.1. Feeding

The form of feeding also plays an important role in the colonization of the intestines of a newborn and infant [8]. Mother's milk is recommended for most newborns. Breastfeeding plays an important role in shaping your baby's gut microbiota [27]. Mother's milk contains health-promoting bacteria that support the primary

colonization of the newborn's intestines. Bifidobacterium, Lactobacillus and representatives of the Enterobacteriaceae family, as well as substances stimulating their growth (prebiotics), including the most important human milk oligosaccharides (HMO), enter the digestive tract of the newborn along with the mother's food. The mixture of protective bacteria, prebiotics with immunoactive proteins in breast milk is responsible for [28]:

1. proper digestion, development of intestinal villi,
2. intestinal peristalsis,
3. shaping the immune system of a newborn.

It has been shown that in breastfed infants, the protective bacteria Bifidobacterium with an admixture of Lactobacillus dominate, while bacteria from the genera Clostridium and Escherichia are much smaller [29–31]. Bacterial diversity grows into an adult microbiota-like syndrome in the first two years of a child's life as a result of exposure to new foods and the microbiota of the child's environment, including siblings, pets and immediate surroundings [32,33]. It should be remembered that an excessive increase in the hygienization of life, resulting in a reduced contact of children with microbes of human and animal origin, and the abuse of antibiotics during pregnancy and the first two years of life, may significantly disturb the development of microbiota [34,35].

2.2. Diet

Diet has a significant influence on the formation of the intestinal microbiota [36]. Therefore, it is important that a woman not only during the entire pregnancy, but also before pregnancy, takes care of a varied, balanced and rich in prebiotics diet [37]. As a result, immune processes are improperly shaped, which can lead to an excessive immune reaction to pollen, dust mites (allergies) or own tissues (autoimmune diseases) [38,39,39]. Additionally, it should be borne in mind that the addition of antibiotics perinatal to the mother or baby and preterm labor strongly influences the microbiota and may have significant consequences for later health [40,41]. Preterm newborns have, inter alia, reduced size of the Bacteroidaceae family in the first months of life and a higher initial percentage of Lactobacillaceae, compared to full-term infants [42].

Antibiotics that are taken perinatally also significantly affect the quantitative and qualitative structure of the intestinal microbiota [43,44] .

The intestinal microbiota forms a kind of ecosystem that is comprehensive and metabolically active. However, he is also very sensitive [45,46]. The factors most strongly disrupting the microbiota include e.g.:

1. incorrect diet low in fiber,
2. antibiotics,
3. proton pump inhibitors,
4. non-steroidal anti-inflammatory drugs,
5. some stress,
6. alcohol,
7. environmental and food pollution.

Studies also show a relationship between intestinal microbiota disorders and civilization diseases, such as type 2 diabetes, obesity and hypertension, the risk of cardiovascular disorders, autoimmune diseases and inflammatory bowel diseases (IBD) [34,47–49].

A very important test is the assessment of the intestinal microbiota, which includes detailed microbiological cultures and genetic analyzes for non-breeding bacteria [50]. Such studies include a detailed qualitative and quantitative analysis of indigenous microorganisms:

1. protective (anaerobic bacteria of the genus *Bacteroides* and *Bifidobacterium*, lactobacilli of the genus *Lactobacillus*)
2. immunostimulatory bacteria (*Enterococcus* and *E. coli*), nourishing the intestinal epithelium (*Faecalibacterium prausnitzii* and *Akkermansia muciniphila*),
3. proteolytic bacteria (*Clostridium*, *Enterobacteriaceae* family including *Klebsiella* spp. *Enterobacter* spp., *Citrobacter* spp., *Proteus* spp.) And *Pseudomonas* and the number of bacteria [51,52].

Non-invasive examination of feces allows for the assessment of the quantitative composition of the intestinal microbiota and enables the selection of the appropriate and most effective, targeted and individualized prebiotic therapy and probiotic therapy [53]. An individually selected diet and probiotics significantly support the intestinal

microbiota. It is also very important to properly select safe, tested preparations. Bacteria should reach the large intestine and stimulate the creation of favorable conditions for the development of normal microbiota [21,54,55].

Helen L. Barrett et al. conducted research that a vegetarian diet is the main determinant of the intestine. They also analyzed the composition of the microbiota in early pregnancy. This study explored the gut microbiota profile in women who were vegetarian or omnivorous in early gestation. Women were selected from participants in the Study of Probiotics in Gestational diabetes (SPRING) randomised controlled trial. Nine women identified as vegetarians were matched to omnivorous women in a 1:2 ratio. Microbiota analyses were performed using 16S rRNA gene amplicon sequencing and analysed using the Quantitative Insights Into Microbial Ecology (QIIME) and Calypso software tools. There was no difference in alpha diversity, but beta diversity was slightly reduced in vegetarians. There were differences seen in the relative abundance of several genera in those on a vegetarian diet, specifically a reduction in *Collinsella*, *Holdemania*, and increases in the relative abundances of *Roseburia* and *Lachnospiraceae*. In this sub-analysis of gut microbiota from women in early pregnancy, a vegetarian as compared to omnivorous diet, was associated with a different gut microbiome, with features suggesting alterations in fermentation end products from a mixed acid fermentation towards more acetate/butyrate [56]. This study explored the gut microbiota profile in women who were vegetarian or omnivorous during early gestation. There was no difference in alpha diversity, but beta diversity was reduced in vegetarians. There were differences seen in the relative abundance of several genera in those on a vegetarian diet, specifically a reduction in *Collinsella*, *Holdemania*, and an increase in *Roseburia* and *Lachnospiraceae*. Functional analyses suggested that women on a vegetarian diet had higher abundance of species involved in fatty acid and lipid synthesis. *Collinsella* is positively correlated with insulin and lipid levels in the SPRING cohort as well as outside pregnancy. In non-pregnant omnivorous people, *Collinsella aerofaciens* was also reported to be higher than in their vegetarian.

4. Discussion

Childbirth is an important stage in the colonization of the human digestive system by the microbiota. Natural childbirth is definitely the most beneficial for the

microbiota, during which the fetus, passing through the genital tract, is populated with the physiological microbiota of the mother's vagina. Numerous studies have shown that in the case of cesarean section, the newborn is colonized by skin bacteria from the mother and hospital staff, and in extreme cases by hospital-derived strains [10,53,57].

Research carried out by Dominguez-Bello found that the microbiota of newborns born physiologically is similar to the microbiota of the vagina with a high proportion of Lactobacillus bacteria, in contrast to those born by caesarean section, whose microbiota contained more skin bacteria, e.g. Streptococcus, Staphylococcus [58]. Unfortunately, the number of imperial burdens is now significantly increasing. Research clearly emphasizes the correlations between cesarean sections and intestinal dysbiosis, which increases the real risk of allergies, atopy, bronchial asthma, type 1 diabetes and obesity later in life [59]. The first 1000 days of a child's life, along with fetal life, programs the microbiota, having a key and long-lasting impact on human development and health [60,61].

5. Summary

In summary, proper nutrition has a major impact on health and well-being during pregnancy. The protection of the intestinal bacterial flora is important during pregnancy. A balanced diet very often covers the increased need for nutrients during pregnancy. Using the right dietary supplements with good bacteria can have significant health benefits for pregnant women and their babies. Probiotic bacteria are live microorganisms which, when administered in appropriate amounts, exert beneficial effects in the host organism. The intestinal microbiota of a pregnant woman has a significant influence on the child's development.

List of references

1. Sergeev, I.N.; Aljutaily, T.; Walton, G.; Huarte, E. Effects of Synbiotic Supplement on Human Gut Microbiota, Body Composition and Weight Loss in Obesity. *Nutrients* 2020, *12*, E222, doi:10.3390/nu12010222.
2. Brink, L.R.; Mercer, K.E.; Piccolo, B.D.; Chintapalli, S.V.; Elolimy, A.; Bowlin, A.K.; Matazel, K.S.; Pack, L.; Adams, S.H.; Shankar, K.; et al. Neonatal Diet

- Alters Fecal Microbiota and Metabolome Profiles at Different Ages in Infants Fed Breast Milk or Formula. *Am. J. Clin. Nutr.* 2020, *111*, 1190–1202, doi:10.1093/ajcn/nqaa076.
3. Gohir, W.; Whelan, F.J.; Surette, M.G.; Moore, C.; Schertzer, J.D.; Sloboda, D.M. Pregnancy-Related Changes in the Maternal Gut Microbiota Are Dependent upon the Mother's Periconceptional Diet. *Gut Microbes* 2015, *6*, 310–320, doi:10.1080/19490976.2015.1086056.
 4. Singh, R.K.; Chang, H.-W.; Yan, D.; Lee, K.M.; Ucmak, D.; Wong, K.; Abrouk, M.; Farahnik, B.; Nakamura, M.; Zhu, T.H.; et al. Influence of Diet on the Gut Microbiome and Implications for Human Health. *J. Transl. Med.* 2017, *15*, 73, doi:10.1186/s12967-017-1175-y.
 5. Ardisson, A.N.; de la Cruz, D.M.; Davis-Richardson, A.G.; Rechcigl, K.T.; Li, N.; Drew, J.C.; Murgas-Torrazza, R.; Sharma, R.; Hudak, M.L.; Triplett, E.W.; et al. Meconium Microbiome Analysis Identifies Bacteria Correlated with Premature Birth. *PLoS One* 2014, *9*, e90784, doi:10.1371/journal.pone.0090784.
 6. Guinane, C.M.; Cotter, P.D. Role of the Gut Microbiota in Health and Chronic Gastrointestinal Disease: Understanding a Hidden Metabolic Organ. *Ther. Adv. Gastroenterol.* 2013, *6*, 295–308, doi:10.1177/1756283X13482996.
 7. Matijašić, M.; Meštrović, T.; Čipčić Paljetak, H.; Perić, M.; Barešić, A.; Verbanac, D. Gut Microbiota beyond Bacteria—Mycobiome, Virome, Archaeome, and Eukaryotic Parasites in IBD. *Int. J. Mol. Sci.* 2020, *21*, 2668, doi:10.3390/ijms21082668.
 8. Houghteling, P.D.; Walker, W.A. Why Is Initial Bacterial Colonization of the Intestine Important to the Infant's and Child's Health? *J. Pediatr. Gastroenterol. Nutr.* 2015, *60*, 294–307, doi:10.1097/MPG.0000000000000597.
 9. Patil, Y.; Gooneratne, R.; Ju, X.-H. Interactions between Host and Gut Microbiota in Domestic Pigs: A Review. *Gut Microbes* *11*, 310–334, doi:10.1080/19490976.2019.1690363.
 10. Neu, J.; Rushing, J. Cesarean versus Vaginal Delivery: Long Term Infant Outcomes and the Hygiene Hypothesis. *Clin. Perinatol.* 2011, *38*, 321–331, doi:10.1016/j.clp.2011.03.008.
 11. Hasan, N.; Yang, H. Factors Affecting the Composition of the Gut Microbiota, and Its Modulation. *PeerJ* 2019, *7*, e7502, doi:10.7717/peerj.7502.
 12. Nishiwaki, H.; Ito, M.; Ishida, T.; Hamaguchi, T.; Maeda, T.; Kashihara, K.; Tsuboi, Y.; Ueyama, J.; Shimamura, T.; Mori, H.; et al. Meta-Analysis of Gut Dysbiosis in Parkinson's Disease. *Mov. Disord. Off. J. Mov. Disord. Soc.* 2020, *35*, 1626–1635, doi:10.1002/mds.28119.
 13. Plaza-Díaz, J.; Álvarez-Mercado, A.I.; Ruiz-Marín, C.M.; Reina-Pérez, I.; Pérez-Alonso, A.J.; Sánchez-Andujar, M.B.; Torné, P.; Gallart-Aragón, T.; Sánchez-Barrón, M.T.; Reyes Lartategui, S.; et al. Association of Breast and Gut Microbiota Dysbiosis and the Risk of Breast Cancer: A Case-Control Clinical Study. *BMC Cancer* 2019, *19*, 495, doi:10.1186/s12885-019-5660-y.

14. Malard, F.; Vekhoff, A.; Lapusan, S.; Isnard, F.; D'incan-Corda, E.; Rey, J.; Saillard, C.; Thomas, X.; Ducastelle-Lepretre, S.; Paubelle, E.; et al. Gut Microbiota Diversity after Autologous Fecal Microbiota Transfer in Acute Myeloid Leukemia Patients. *Nat. Commun.* 2021, *12*, 3084, doi:10.1038/s41467-021-23376-6.
15. Basolo, A.; Hohenadel, M.; Ang, Q.Y.; Piaggi, P.; Heinitz, S.; Walter, M.; Walter, P.; Parrington, S.; Trinidad, D.D.; von Schwartzberg, R.J.; et al. Effects of Underfeeding and Oral Vancomycin on Gut Microbiome and Nutrient Absorption in Humans. *Nat. Med.* 2020, *26*, 589–598, doi:10.1038/s41591-020-0801-z.
16. Boonstra, E.; de Kleijn, R.; Colzato, L.S.; Alkemade, A.; Forstmann, B.U.; Nieuwenhuis, S. Neurotransmitters as Food Supplements: The Effects of GABA on Brain and Behavior. *Front. Psychol.* 2015, *6*, 1520, doi:10.3389/fpsyg.2015.01520.
17. Cepeda, M.S.; Katz, E.G.; Blacketer, C. Microbiome-Gut-Brain Axis: Probiotics and Their Association With Depression. *J. Neuropsychiatry Clin. Neurosci.* 2017, *29*, 39–44, doi:10.1176/appi.neuropsych.15120410.
18. Cryan, J.F.; Dinan, T.G. Mind-Altering Microorganisms: The Impact of the Gut Microbiota on Brain and Behaviour. *Nat. Rev. Neurosci.* 2012, *13*, 701–712, doi:10.1038/nrn3346.
19. Khor, B.; Gardet, A.; Xavier, R.J. Genetics and Pathogenesis of Inflammatory Bowel Disease. *Nature* 2011, *474*, 307–317, doi:10.1038/nature10209.
20. Kasper, L.H. The Evolving Role of the Gut Microbiome in Human Disease. *FEBS Lett.* 2014, *588*, 4101, doi:10.1016/j.febslet.2014.09.015.
21. Kim, C.-S.; Cha, L.; Sim, M.; Jung, S.; Chun, W.Y.; Baik, H.W.; Shin, D.-M. Probiotic Supplementation Improves Cognitive Function and Mood with Changes in Gut Microbiota in Community-Dwelling Older Adults: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. *J. Gerontol. A. Biol. Sci. Med. Sci.* 2021, *76*, 32–40, doi:10.1093/gerona/glaa090.
22. Cryan, J.F.; O'Riordan, K.J.; Cowan, C.S.M.; Sandhu, K.V.; Bastiaanssen, T.F.S.; Boehme, M.; Codagnone, M.G.; Cussotto, S.; Fulling, C.; Golubeva, A.V.; et al. The Microbiota-Gut-Brain Axis. *Physiol. Rev.* 2019, *99*, 1877–2013, doi:10.1152/physrev.00018.2018.
23. Abrahamsson, T.R.; Wu, R.Y.; Jenmalm, M.C. Gut Microbiota and Allergy: The Importance of the Pregnancy Period. *Pediatr. Res.* 2015, *77*, 214–219, doi:10.1038/pr.2014.165.
24. Arboleya, S.; Sánchez, B.; Milani, C.; Duranti, S.; Solís, G.; Fernández, N.; de los Reyes-Gavilán, C.G.; Ventura, M.; Margolles, A.; Gueimonde, M. Intestinal Microbiota Development in Preterm Neonates and Effect of Perinatal Antibiotics. *J. Pediatr.* 2015, *166*, 538–544, doi:10.1016/j.jpeds.2014.09.041.
25. Hurley, E.; Mullins, D.; Barrett, M.P.; O'Shea, C.A.; Kinirons, M.; Ryan, C.A.; Stanton, C.; Whelton, H.; Harris, H.M.B.; O'Toole, P.W. The Microbiota of the Mother at Birth and Its Influence on the Emerging Infant Oral Microbiota from

- Birth to 1 Year of Age: A Cohort Study. *J. Oral Microbiol.* 2019, *11*, 1599652, doi:10.1080/20002297.2019.1599652.
26. Koedooder, R.; Mackens, S.; Budding, A.; Fares, D.; Blockeel, C.; Laven, J.; Schoenmakers, S. Identification and Evaluation of the Microbiome in the Female and Male Reproductive Tracts. *Hum. Reprod. Update* 2019, *25*, 298–325, doi:10.1093/humupd/dmy048.
 27. Ford, S.L.; Lohmann, P.; Preidis, G.A.; Gordon, P.S.; O'Donnell, A.; Hagan, J.; Venkatachalam, A.; Balderas, M.; Luna, R.A.; Hair, A.B. Improved Feeding Tolerance and Growth Are Linked to Increased Gut Microbial Community Diversity in Very-Low-Birth-Weight Infants Fed Mother's Own Milk Compared with Donor Breast Milk. *Am. J. Clin. Nutr.* 2019, *109*, 1088–1097, doi:10.1093/ajcn/nqz006.
 28. Le Doare, K.; Holder, B.; Bassett, A.; Pannaraj, P.S. Mother's Milk: A Purposeful Contribution to the Development of the Infant Microbiota and Immunity. *Front. Immunol.* 2018, *9*, 361, doi:10.3389/fimmu.2018.00361.
 29. Wall, R.; Ross, R.P.; Ryan, C.A.; Hussey, S.; Murphy, B.; Fitzgerald, G.F.; Stanton, C. Role of Gut Microbiota in Early Infant Development. *Clin. Med. Pediatr.* 2009, *3*, 45–54.
 30. Martin, R.; Makino, H.; Cetinyurek Yavuz, A.; Ben-Amor, K.; Roelofs, M.; Ishikawa, E.; Kubota, H.; Swinkels, S.; Sakai, T.; Oishi, K.; et al. Early-Life Events, Including Mode of Delivery and Type of Feeding, Siblings and Gender, Shape the Developing Gut Microbiota. *PLoS ONE* 2016, *11*, e0158498, doi:10.1371/journal.pone.0158498.
 31. Laursen, M.F.; Sakanaka, M.; von Burg, N.; Mörbe, U.; Andersen, D.; Moll, J.M.; Pekmez, C.T.; Rivollier, A.; Michaelsen, K.F.; Mølgaard, C.; et al. Bifidobacterium Species Associated with Breastfeeding Produce Aromatic Lactic Acids in the Infant Gut. *Nat. Microbiol.* 2021, *6*, 1367–1382, doi:10.1038/s41564-021-00970-4.
 32. Tun, H.M.; Konya, T.; Takaro, T.K.; Brook, J.R.; Chari, R.; Field, C.J.; Guttman, D.S.; Becker, A.B.; Mandhane, P.J.; Turvey, S.E.; et al. Exposure to Household Furry Pets Influences the Gut Microbiota of Infants at 3–4 Months Following Various Birth Scenarios. *Microbiome* 2017, *5*, 40, doi:10.1186/s40168-017-0254-x.
 33. Ronan, V.; Yeasin, R.; Claud, E.C. Childhood Development and the Microbiome: The Intestinal Microbiota in Maintenance of Health and Development of Disease During Childhood Development. *Gastroenterology* 2021, *160*, 495–506, doi:10.1053/j.gastro.2020.08.065.
 34. Wilkins, A.T.; Reimer, R.A. Obesity, Early Life Gut Microbiota, and Antibiotics. *Microorganisms* 2021, *9*, 413, doi:10.3390/microorganisms9020413.
 35. Mueller, N.T.; Bakacs, E.; Combellick, J.; Grigoryan, Z.; Dominguez-Bello, M.G. The Infant Microbiome Development: Mom Matters. *Trends Mol. Med.* 2015, *21*, 109–117, doi:10.1016/j.molmed.2014.12.002.

36. Leeming, E.R.; Johnson, A.J.; Spector, T.D.; Le Roy, C.I. Effect of Diet on the Gut Microbiota: Rethinking Intervention Duration. *Nutrients* 2019, *11*, 2862, doi:10.3390/nu11122862.
37. Conlon, M.A.; Bird, A.R. The Impact of Diet and Lifestyle on Gut Microbiota and Human Health. *Nutrients* 2014, *7*, 17–44, doi:10.3390/nu7010017.
38. Jacquet, A. Innate Immune Responses in House Dust Mite Allergy. *ISRN Allergy* 2013, *2013*, 735031, doi:10.1155/2013/735031.
39. Pascal, M.; Perez-Gordo, M.; Caballero, T.; Escribese, M.M.; Lopez Longo, M.N.; Luengo, O.; Manso, L.; Matheu, V.; Seoane, E.; Zamorano, M.; et al. Microbiome and Allergic Diseases. *Front. Immunol.* 2018, *9*, 1584, doi:10.3389/fimmu.2018.01584.
40. Zhou, P.; Zhou, Y.; Liu, B.; Jin, Z.; Zhuang, X.; Dai, W.; Yang, Z.; Feng, X.; Zhou, Q.; Liu, Y.; et al. Perinatal Antibiotic Exposure Affects the Transmission between Maternal and Neonatal Microbiota and Is Associated with Early-Onset Sepsis. *mSphere* 2020, *5*, e00984-19, doi:10.1128/mSphere.00984-19.
41. Yang, I.; Corwin, E.J.; Brennan, P.A.; Jordan, S.; Murphy, J.R.; Dunlop, A. The Infant Microbiome: Implications for Infant Health and Neurocognitive Development. *Nurs. Res.* 2016, *65*, 76–88, doi:10.1097/NNR.0000000000000133.
42. Oliphant, K.; Ali, M.; D’Souza, M.; Hughes, P.D.; Sulakhe, D.; Wang, A.Z.; Xie, B.; Yeasin, R.; Msall, M.E.; Andrews, B.; et al. Bacteroidota and Lachnospiraceae Integration into the Gut Microbiome at Key Time Points in Early Life Are Linked to Infant Neurodevelopment. *Gut Microbes* *13*, 1997560, doi:10.1080/19490976.2021.1997560.
43. Ainonen, S.; Tejesvi, M.V.; Mahmud, M.R.; Paalanne, N.; Pokka, T.; Li, W.; Nelson, K.E.; Salo, J.; Renko, M.; Vänni, P.; et al. Antibiotics at Birth and Later Antibiotic Courses: Effects on Gut Microbiota. *Pediatr. Res.* 2022, *91*, 154–162, doi:10.1038/s41390-021-01494-7.
44. Kwon, Y.; Cho, Y.-S.; Lee, Y.-M.; Kim, S.; Bae, J.; Jeong, S.-J. Changes to Gut Microbiota Following Systemic Antibiotic Administration in Infants. *Antibiotics* 2022, *11*, 470, doi:10.3390/antibiotics11040470.
45. Thursby, E.; Juge, N. Introduction to the Human Gut Microbiota. *Biochem. J.* 2017, *474*, 1823–1836, doi:10.1042/BCJ20160510.
46. Strzępa, A.; Szczepanik, M. [Influence of natural gut flora on immune response]. *Postępy Hig. Med. Doswiadczalnej Online* 2013, *67*, 908–920, doi:10.5604/17322693.1064563.
47. Ferrocino, I.; Ponzio, V.; Gambino, R.; Zarovska, A.; Leone, F.; Monzeglio, C.; Goitre, I.; Rosato, R.; Romano, A.; Grassi, G.; et al. Changes in the Gut Microbiota Composition during Pregnancy in Patients with Gestational Diabetes Mellitus (GDM). *Sci. Rep.* 2018, *8*, 12216, doi:10.1038/s41598-018-30735-9.
48. Giuliani, C.; Sciacca, L.; Biase, N.D.; Tumminia, A.; Milluzzo, A.; Faggiano, A.; Romana Amorosi, F.; Convertino, A.; Bitterman, O.; Festa, C.; et al. Gestational

- Diabetes Mellitus Pregnancy by Pregnancy: Early, Late and Nonrecurrent GDM. *Diabetes Res. Clin. Pract.* 2022, 188, 109911, doi:10.1016/j.diabres.2022.109911.
49. Changes in the Gut Microbiota Composition during Pregnancy in Patients with Gestational Diabetes Mellitus (GDM) - PMC Available online: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6093919/> (accessed on 13 June 2022).
 50. Hiergeist, A.; Gläsner, J.; Reischl, U.; Gessner, A. Analyses of Intestinal Microbiota: Culture versus Sequencing. *ILAR J.* 2015, 56, doi:10.1093/ilar/ilv017.
 51. Fijan, S. Microorganisms with Claimed Probiotic Properties: An Overview of Recent Literature. *Int. J. Environ. Res. Public Health* 2014, 11, 4745–4767, doi:10.3390/ijerph110504745.
 52. Yaghoubar, R.; Behrouzi, A.; Fateh, A.; Nojoumi, S.A.; Vaziri, F.; Khatami, S.; Siadat, S.D. Effects of Akkermansia Muciniphila and Faecalibacterium Prausnitzii on Serotonin Transporter Expression in Intestinal Epithelial Cells. *J. Diabetes Metab. Disord.* 2021, 20, 1–5, doi:10.1007/s40200-020-00539-8.
 53. Dominguez-Bello, M.G.; De Jesus-Laboy, K.M.; Shen, N.; Cox, L.M.; Amir, A.; Gonzalez, A.; Bokulich, N.A.; Song, S.J.; Hoashi, M.; Rivera-Vina, J.I.; et al. Partial Restoration of the Microbiota of Cesarean-Born Infants via Vaginal Microbial Transfer. *Nat. Med.* 2016, 22, 250–253, doi:10.1038/nm.4039.
 54. SUVOROV, A. Gut Microbiota, Probiotics, and Human Health. *Biosci. Microbiota Food Health* 2013, 32, 81–91, doi:10.12938/bmfh.32.81.
 55. Hempel, S.; Newberry, S.J.; Maher, A.R.; Wang, Z.; Miles, J.N.V.; Shanman, R.; Johnsen, B.; Shekelle, P.G. Probiotics for the Prevention and Treatment of Antibiotic-Associated Diarrhea: A Systematic Review and Meta-Analysis. *JAMA* 2012, 307, 1959–1969, doi:10.1001/jama.2012.3507.
 56. Barrett, H.; Gomez-Arango, L.; Wilkinson, S.; McIntyre, H.; Callaway, L.; Morrison, M.; Dekker Nitert, M. A Vegetarian Diet Is a Major Determinant of Gut Microbiota Composition in Early Pregnancy. *Nutrients* 2018, 10, 890, doi:10.3390/nu10070890.
 57. Ravel, J.; Gajer, P.; Abdo, Z.; Schneider, G.M.; Koenig, S.S.K.; McCulle, S.L.; Karlebach, S.; Gorle, R.; Russell, J.; Tacket, C.O.; et al. Vaginal Microbiome of Reproductive-Age Women. *Proc. Natl. Acad. Sci. U. S. A.* 2011, 108 Suppl 1, 4680–4687, doi:10.1073/pnas.1002611107.
 58. Dominguez-Bello, M.G.; Costello, E.K.; Contreras, M.; Magris, M.; Hidalgo, G.; Fierer, N.; Knight, R. Delivery Mode Shapes the Acquisition and Structure of the Initial Microbiota across Multiple Body Habitats in Newborns. *Proc. Natl. Acad. Sci. U. S. A.* 2010, 107, 11971–11975, doi:10.1073/pnas.1002601107.
 59. Arrieta, M.-C.; Stiemsma, L.T.; Dimitriu, P.A.; Thorson, L.; Russell, S.; Yurist-Doutsch, S.; Kuzeljevic, B.; Gold, M.J.; Britton, H.M.; Lefebvre, D.L.; et al. Early Infancy Microbial and Metabolic Alterations Affect Risk of Childhood Asthma. *Sci. Transl. Med.* 2015, 7, doi:10.1126/scitranslmed.aab2271.

60. Chen, H.J.; Gur, T.L. Intrauterine Microbiota: Missing, or the Missing Link? *Trends Neurosci.* 2019, *42*, 402–413, doi:10.1016/j.tins.2019.03.008.
61. Auriemma, R.S.; Sciarati, R.; del Vecchio, G.; Liccardi, A.; Verde, N.; Pirchio, R.; Pivonello, R.; Ercolini, D.; Colao, A. The Vaginal Microbiome: A Long Urogenital Colonization Throughout Woman Life. *Front. Cell. Infect. Microbiol.* 2021, *11*, 686167, doi:10.3389/fcimb.2021.686167.