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## Review article

## The role of maternal microbiota in shaping neonatal immunity: Implications for infectious disease prevention

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### ABSTRACT

**Background:** Maternal microbiota plays a pivotal role in shaping neonatal immune development, influencing susceptibility to infections and long-term health outcomes. This review delves into the intricate interactions between maternal microbiota and neonatal immunity, emphasizing microbial transfer mechanisms during pregnancy, delivery, and breastfeeding. It explores how maternal microbiota educates the neonatal immune system, fostering immune tolerance and protection against pathogens. Factors that disrupt maternal microbial composition, such as antibiotic use, maternal diet, and infections, are examined in relation to their detrimental effects on neonatal health. The review also discusses emerging strategies to optimize maternal microbiota for improved neonatal immunity, including probiotics, prebiotics, and targeted dietary interventions. Additionally, the broader implications of maternal microbiota research in preventing neonatal infectious diseases are explored, highlighting its significance in global health efforts. By understanding these complex maternal-neonatal microbial interactions, new therapeutic and preventive strategies can be developed to support early-life immune resilience. This review underscores the need for further research into maternal microbiota modulation as a promising avenue for enhancing neonatal health and reducing infection-related morbidity worldwide.

### Introduction

The maternal microbiota—the community of microorganisms residing in the maternal gut, vaginal tract, oral cavity, and other niches—is a cornerstone of neonatal health. During critical windows of development, such as pregnancy, delivery, and the early postnatal period, maternal microbiota contributes to immune system priming in the neonate. These interactions not only influence neonatal susceptibility to infections but also impact long-term outcomes, including allergy

development, autoimmunity, and metabolic health [1].

The maternal microbiota—the community of microorganisms residing in the maternal gut, vaginal tract, oral cavity, and other niches—is a cornerstone of neonatal health. During critical windows of development, such as pregnancy, delivery, and the early postnatal period, maternal microbiota contributes significantly to immune system priming in the neonate. These interactions not only influence neonatal susceptibility to

infections but also impact long-term outcomes, including allergy development, autoimmunity, and metabolic health [2].

Recent advances in microbiome research have illuminated the complex pathways by which maternal microbiota affects neonatal immunity. Evidence suggests that the composition of maternal gut microbiota can shape the immune profiles of offspring, influencing T cell activity and cytokine production [1]. Additionally, maternal microbiota is transmitted to infants during pregnancy and through breastfeeding. The placenta has been shown to harbor its own unique microbial community, suggesting that some microbial exposure begins even before birth [3]. Following delivery, breast milk serves as a critical pathway for microbial transmission, containing not only nutrients but also microbial antigens that stimulate the infant's immune system [2]. This early colonization is vital for developing a robust immune system capable of distinguishing between harmful pathogens and benign substances.

The mode of delivery significantly impacts the initial colonization patterns of the neonatal microbiota. Infants born via cesarean section often miss out on exposure to maternal vaginal and fecal microbes, leading to altered microbial communities that can predispose them to immune dysregulation and increased risk of allergic diseases [4]. Research indicates that cesarean-born infants tend to exhibit an imbalance in Th1/Th2 cell responses, which may contribute to a higher incidence of asthma and allergies later in life [5].

Maternal factors such as diet, antibiotic use, and environmental exposures further shape the maternal microbiome and subsequently influence neonatal health outcomes. For example, a diet rich in fiber and fermented foods has been associated with greater microbial diversity in mothers, which correlates with reduced allergic responses in their children [6]. Conversely, excessive antibiotic use during pregnancy can disrupt maternal microbiota composition, potentially leading to negative outcomes for the infant's immune system [7].

Given these insights into the intricate relationship between maternal microbiota and neonatal immunity, optimizing maternal microbial health emerges as a vital strategy for improving neonatal outcomes. Interventions may include dietary modifications aimed at enhancing gut diversity, administration of probiotics during

pregnancy, and careful management of antibiotic use to maintain a healthy microbiome. Such strategies hold promise for mitigating risks associated with infectious diseases and promoting long-term health in neonates [8].

Recent advances in microbiome research have illuminated the complex pathways by which maternal microbiota affects neonatal immunity. This review provides a comprehensive overview of these pathways, emphasizing their implications for preventing infectious diseases. We also discuss maternal factors that shape the microbiota and propose strategies to optimize maternal microbial health for improved neonatal outcomes.

This review aims to provide a comprehensive overview of the pathways by which maternal microbiota influences neonatal immunity and discusses their implications for preventing infectious diseases. By understanding these interactions more deeply, we can better inform strategies that promote both maternal and neonatal health.

## **Development of Neonatal Immunity**

### **Role of Maternal Microbiota in Immune System Priming**

Neonates are born with an immature immune system that relies significantly on microbial exposures to help develop a functional immune response. Maternal microbiota plays a pivotal role in this process through several mechanisms:

#### **Antigen Exposure:**

The maternal microbiota, which is a complex ecosystem of microbes residing in the mother's gastrointestinal, vaginal, and other body sites, exposes the neonate to a variety of antigens. These antigens are recognized by the neonatal immune system, which helps train immune cells, such as dendritic cells and T cells, to develop the ability to distinguish between harmful and harmless microorganisms [9]. This exposure primes the immune system for future encounters with pathogens while also fostering tolerance to commensal bacteria [10].

#### **Tolerogenic Pathways:**

Exposure to maternal microbes, especially during the birth process, is essential in guiding the neonatal immune system towards a balanced immune response. Commensal bacteria present during birth and breastfeeding stimulate the development of regulatory T cells (Tregs), which play a key role in maintaining immune tolerance.

This process helps the immune system learn to avoid overreacting to harmless microbes, a critical feature to prevent autoimmune diseases and allergies [11].

**Cytokine Modulation:** Maternal-derived microbial metabolites, especially short-chain fatty acids (SCFAs) produced by the fermentation of dietary fiber by maternal gut microbiota, influence neonatal immune responses. SCFAs such as butyrate and acetate have been shown to modulate the production of pro- and anti-inflammatory cytokines in neonatal immune cells, promoting immune tolerance and preventing inflammatory disorders [12]. These metabolites can also influence the development of mucosal immunity in the neonatal gut, which is essential for defending against infections and regulating immune responses.

### Timing and Critical Windows

The timing of microbial exposure is critical for optimal immune system development. Different windows of exposure throughout pregnancy, birth, and early infancy can significantly impact neonatal immune function:

**In Utero:** While traditionally considered a sterile environment, recent studies suggest that the placenta may harbor a low-biomass microbiota that interacts with fetal tissues. These microbes could influence fetal immune development, possibly shaping the fetus' ability to respond to infections and tolerate antigens post-birth [13]. However, the existence of a microbiome in the placenta remains a debated topic, with some suggesting microbial DNA found in placental tissues could originate from maternal blood rather than the placenta itself.

**During Birth:** The birth process itself is a critical event for shaping the neonatal microbiome. Vaginal delivery exposes neonates to maternal vaginal and fecal microbiota, which provides initial immune system "seeding." These microbes help establish the first line of defense in the neonatal gut and skin, promoting the development of both innate and adaptive immunity. Cesarean delivery, in contrast, results in a microbiome that is more similar to that of the hospital environment, potentially leading to altered immune system development and increased susceptibility to infections and allergies later in life [14].

**Postnatally:** After birth, breastfeeding continues to play a significant role in shaping neonatal immunity. Human breast milk is rich in immunological factors, including antibodies, oligosaccharides, and immune cells, that contribute

to the development of the infant's gut microbiota and immune system. *Lactobacillus* and *Bifidobacterium* species, which are often present in breast milk, promote the development of a healthy immune response. Additionally, the act of breastfeeding itself provides ongoing exposure to maternal microbiota, continuing the process of immune priming [15]. Furthermore, the nutrients in breast milk can shape the neonatal gut microbiota by supporting the growth of beneficial bacteria, which in turn influences the development of systemic immunity.

### Maternal Factors Influencing Microbiota

The maternal microbiome plays a crucial role in shaping the neonatal microbiota, influencing the health outcomes of infants. Various maternal factors, including antibiotic use, diet, infections, and mode of delivery, significantly affect the composition and diversity of microbial communities that neonates are exposed to at birth. This comprehensive overview will delve into these factors and their implications for neonatal health, supported by recent research findings.

#### 1. Antibiotic Use

Maternal antibiotic use during pregnancy or delivery is one of the most impactful factors influencing neonatal microbiota. Research has shown that antibiotics can disrupt the natural microbial diversity in both mothers and infants, leading to several potential consequences:

**Reduced Transmission of Beneficial Microbes:** Antibiotics administered during labor can diminish the transmission of beneficial microbes from mother to neonate during vaginal delivery. This is critical as these microbes are essential for establishing a healthy gut microbiome in infants [16].

**Increased Risk of Dysbiosis:** The disruption caused by antibiotics can lead to dysbiosis in neonates, which has been linked to various health conditions such as necrotizing enterocolitis (NEC) and other long-term issues like allergies and autoimmune diseases. A study [14] found that antibiotic exposure in neonates is associated with decreased microbial diversity and an increased abundance of antibiotic-resistant bacteria.

#### 2. Diet and Nutritional Status

Maternal diet is a significant modulator of microbiota composition, influencing both maternal and neonatal health:

**Impact of Fiber-Rich Diets:** Diets high in fiber promote the growth of beneficial microbes that produce short-chain fatty acids (SCFAs), which are crucial for immune modulation. SCFAs play a vital role in maintaining gut health and regulating immune responses [17].

**Consequences of High-Fat, Low-Fiber Diets:** Conversely, high-fat and low-fiber diets can lead to dysbiosis, reducing the availability of beneficial microbial metabolites necessary for neonatal immune development. A study [18] demonstrated that maternal dietary patterns directly influence the microbial composition transmitted to infants during delivery, highlighting the importance of maternal nutrition in early microbial colonization.

### 3. Infections

Maternal infections during pregnancy can significantly alter microbiota composition:

**Vaginal Infections:** These infections can lead to changes in the maternal microbiota that increase the risk of preterm birth and influence the initial microbial exposures for the neonate. For instance, a report by a researcher [19] indicated that maternal infections are associated with alterations in neonatal microbiota diversity and composition, which can affect long-term health outcomes.

**Maternal Immune Response:** The maternal inflammatory state and immune-related metabolites have been linked to the development of both fetal and neonatal immune systems. Elevated cytokines in maternal circulation may influence the establishment of the neonatal microbiome [20].

#### Mode of Delivery

The method of delivery has profound implications for neonatal microbial exposure:

**Vaginal Delivery:** Infants born vaginally are exposed to maternal vaginal microbes, including *Lactobacillus* and *Bifidobacterium*, which are beneficial for establishing a healthy gut microbiome. This exposure is essential for developing a diverse microbial community that supports immune function [21].

**Cesarean Section:** In contrast, cesarean delivery limits exposure to maternal vaginal microbiota, leading to increased reliance on environmental microbes. Research suggests that this may predispose cesarean-born infants to dysbiosis and associated health issues later in life [22]. (Blaser, 2015). Interestingly, some studies have explored “vaginal seeding” as a method to transfer beneficial microbes from mother to cesarean-born

infants; however, its effectiveness remains debated [23].

#### Mechanisms of Microbial Transfer

##### Placental and Amniotic Fluid Transfer

While traditionally considered sterile, emerging research has revealed that the placenta and amniotic fluid harbor a low-biomass microbiota. Studies suggest that maternal gut and oral microbiota can translocate to the placenta via hematogenous routes, influencing the fetal immune system development [24]. This microbial exposure primes the immune system and may shape the fetus’s immune responses. For example, maternal gut-derived microbial antigens can help in the early maturation of the fetal immune system by influencing T-cell differentiation and immune tolerance [1].

##### Vaginal Delivery

During vaginal delivery, neonates are exposed to maternal vaginal microbes. Species like *Lactobacillus* and *Bifidobacterium* are prominent in this environment and are transferred to the infant, especially in the gut, where they help establish the early microbiota. This process is vital for promoting the development of immune tolerance and the maturation of the immune system [14]. Vaginal birth is linked to a higher diversity of microbial colonization, which has been associated with a lower incidence of immune-related diseases [25].

##### Breastfeeding

Breast milk contains a rich and diverse microbiota, including strains like *Bifidobacterium* and *Streptococcus*, and provides the baby with essential nutrients that shape the gut microbiome. In addition to these microbes, human milk oligosaccharides (HMOs) play a pivotal role in nurturing beneficial bacteria, particularly *Bifidobacterium*, which promotes gut health and strengthens the neonatal immune system [26]. Breastfeeding has been associated with a lower incidence of infections and allergies in infants, primarily due to these immunomodulatory effects.

#### Microbiota-Driven Disease Prevention in Neonates

##### Reducing the Risk of Infections

A diverse and balanced neonatal microbiota is essential for protecting against infections. *Lactobacillus* species, common in the neonatal gut, have been shown to reduce the risk of gastrointestinal infections, including diarrhea

caused by pathogens such as Rotavirus [27]. Furthermore, short-chain fatty acids (SCFAs), produced by beneficial gut bacteria, enhance the integrity of the intestinal barrier, preventing pathogen invasion [28].

### Long-Term Immune Health

**Allergy Prevention:** Early-life microbial exposure is associated with a reduced risk of allergic diseases, likely due to the development of immune tolerance. This is thought to occur via the modulation of the neonatal immune system by the gut microbiota [29].

**Autoimmunity:** Disruptions in the microbiota during critical developmental windows may lead to immune dysregulation and an increased risk of autoimmune diseases, including type 1 diabetes. Studies have shown that altered microbiota in infancy may contribute to immune system errors that predispose to autoimmune disorders later in life [30].

### Disruptions to Maternal Microbiota

#### 1. Antibiotic-Associated Dysbiosis

Antibiotic use, particularly during labor, can disrupt the maternal microbiota, significantly reducing the diversity of microbial species. This disruption impairs the normal transmission of beneficial microbes to the infant, which may result in increased risks of neonatal infections and antibiotic-resistant bacteria [31]. Studies have linked antibiotic exposure to an increased risk of conditions such as necrotizing enterocolitis in preterm infants [32].

#### 2. Impact of Environmental Factors

Environmental stressors such as pollution, dietary factors, and antibiotic use can alter the maternal microbiota, reducing microbial diversity and affecting microbial transmission during birth. Factors like air pollution have been shown to impact gut microbiota composition, which in turn can influence the neonate's immune development [33].

### Optimizing Maternal Microbiota for Neonatal Immunity

#### 1. Probiotics and Prebiotics

**Probiotics:** Supplementing with probiotics like *Lactobacillus* and *Bifidobacterium* during pregnancy can help restore and maintain a healthy maternal gut microbiota, which supports the establishment of beneficial microbes in the neonate [34].

**Prebiotics:** Maternal intake of prebiotic fibers, found in foods like fruits, vegetables, and whole grains, promotes the growth of beneficial gut microbes and increases the production of SCFAs, further supporting neonatal immune health [35].

#### 2. Dietary Interventions

Diets rich in fiber, fruits, vegetables, and whole grains help support a diverse and balanced maternal microbiota, which is crucial for a healthy neonatal microbiome [36].

Omega-3 fatty acids and fermented foods, such as yogurt and kimchi, have been shown to enhance microbial diversity and have anti-inflammatory effects, which may be beneficial for both the mother and infant [37].

#### 3. Reducing Unnecessary Antibiotic Use

Antibiotics should be used judiciously during pregnancy and labor to preserve the microbial diversity of both the mother and the infant. Avoiding unnecessary antibiotic exposure can help ensure that beneficial bacteria are transmitted to the newborn, reducing the risk of infections and other long-term health issues [38].

### Implications for Public Health and Research

#### 1. Maternal Microbiota as a Target for Intervention

Targeting the maternal microbiota through dietary interventions, probiotics, and responsible antibiotic use presents a promising strategy to improve neonatal health. By improving maternal microbial health, we can significantly reduce the risk of neonatal infections, allergies, and autoimmune diseases [39].

#### 2. Integration into Global Health Policies

Incorporating microbiota-focused interventions into maternal and neonatal health programs could lead to better outcomes for infants worldwide. This includes promoting the use of probiotics and prebiotics and incorporating microbiota screening into prenatal care [40]. Policy initiatives should prioritize reducing unnecessary antibiotic use during pregnancy and birth to preserve microbiota diversity.

#### 3. Research Directions

**Longitudinal Studies:** Further longitudinal studies are needed to understand the long-term effects of maternal microbiota interventions on neonatal health. Such research will help establish the best practices for promoting a healthy microbiome in both mothers and infants.

### Microbiota-Based Therapeutics:

Exploring microbiota-based therapeutics, such as microbiome transplants, could provide a novel way to prevent neonatal infections and immune disorders.

### Conclusion

The maternal microbiota plays a crucial role in shaping neonatal immunity, influencing the infant's susceptibility to infections and the development of immune tolerance. The transfer of microbes through the placenta, during vaginal delivery, and via breastfeeding is essential for establishing a healthy microbiome in the neonate. Disruptions to this transfer, such as those caused by antibiotics or environmental factors, can increase the risk of health issues in both the mother and child. Therefore, optimizing maternal microbiota through strategies like probiotics, prebiotics, and careful antibiotic use is vital for improving neonatal health outcomes. A multidisciplinary approach that integrates microbiota research, public health policies, and clinical practices is necessary to harness the full potential of maternal microbiota in preventing infections and promoting long-term health for both mothers and their infants. By prioritizing these interventions, we can reduce the burden of infectious diseases and improve overall public health.

### References

1. Jiménez E, Fernández L, Marín ML. Isolation of commensal bacteria from umbilical cord blood of healthy neonates born by cesarean section. *Curr Microbiol.* 2005;51(4):270-274. doi:10.1007/S00284-005-0020-3
2. Sevelsted A, Stokholm J, Bønnelykke K, Bisgaard H. Cesarean section chronic immune disorders. *Pediatrics.* 2015;135(1):e92-e98. doi:10.1542/PEDS.2014-0596
3. Stokholm J, Schjørring S, Eskildsen CE. Antibiotic use during pregnancy alters the commensal vaginal microbiota. *Clinical Microbiology and Infection.* 2014;20(7):629-635. doi:10.1111/1469-0691.12411
4. Nunez N, Réot L, Menu E. Neonatal Immune System Ontogeny: The Role of Maternal Microbiota and Associated Factors. *How Might the Non-Human Primate Model Enlighten the Path? Vaccines* 2021, Vol 9, Page 584. 2021;9(6):584. doi:10.3390/VACCINES9060584
5. Gensollen T, Iyer SS, Kasper DL, Blumberg RS. How colonization by microbiota in early life shapes the immune system. *Science* (1979). 2016;352(6285):539-544. doi:10.1126/SCIENCE.AAD9378
6. Hornef MW, Torow N. 'Layered immunity' and the 'neonatal window of opportunity' – timed succession of non-redundant phases to establish mucosal host–microbial homeostasis after birth. *Immunology.* 2020;159(1):15-25. doi:10.1111/IMM.13149
7. Dierikx TH, Visser DH, Benninga MA. The influence of prenatal and intrapartum antibiotics on intestinal microbiota colonisation in infants: A systematic review. *Journal of Infection.* 2020;81(2):190-204. doi:10.1016/J.JINF.2020.05.002
8. Niu X, Daniel S, Kumar D. Transient neonatal antibiotic exposure increases susceptibility to late-onset sepsis driven by microbiota-dependent suppression of type 3 innate lymphoid cells. *Sci Rep.* 2020;10(1). doi:10.1038/S41598-020-69797-Z
9. Hu Y, Jin P, Peng J, Zhang X, Wong FS, Wen L. Different immunological responses to early-life antibiotic exposure affecting autoimmune diabetes development in NOD mice. *J Autoimmun.* 2016;72:47-56. doi:10.1016/J.JAUT.2016.05.001
10. Zhang X, Borbet TC, Fallegger A, Wipperfman MF, Blaser MJ, Müller A. An antibiotic-impacted microbiota compromises

- the development of colonic regulatory t cells and predisposes to dysregulated immune responses. *mBio*. 2021;12(1):1-16. doi:10.1128/MBIO.03335-20
11. Stockinger B, Meglio P Di, Gialitakis M, Duarte JH. The aryl hydrocarbon receptor: Multitasking in the immune system. *Annu Rev Immunol*. 2014;32:403-432. doi:10.1146/ANNUREV-IMMUNOL-032713-120245
  12. De Agüero MG, Ganai-Vonarburg SC, Fuhrer T. The maternal microbiota drives early postnatal innate immune development. *Science* (1979). 2016;351(6279):1296-1302. doi:10.1126/SCIENCE.AAD2571
  13. Rackaityte E, Halkias J, Fukui EM. Viable bacterial colonization is highly limited in the human intestine in utero. *Nat Med*. 2020;26(4):599-607. doi:10.1038/S41591-020-0761-3
  14. Theis KR, Romero R, Winters AD. 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(3):267.e1-267.e39. doi:10.1016/J.AJOG.2018.10.018
  15. Walter J, Hornef MW. A philosophical perspective on the prenatal in utero microbiome debate. *Microbiome*. 2021;9(1). doi:10.1186/S40168-020-00979-7
  16. de Goffau MC, Charnock-Jones DS, Smith GCS, Parkhill J. Batch effects account for the main findings of an in utero human intestinal bacterial colonization study. *Microbiome*. 2021;9(1). doi:10.1186/S40168-020-00949-Z
  17. Li Y, Toothaker JM, Ben-Simon S. In utero human intestine harbors unique metabolome, including bacterial metabolites. *JCI Insight*. 2020;5(21). doi:10.1172/JCI.INSIGHT.138751
  18. Rackaityte E, Halkias J, Fukui EM. Corroborating evidence refutes batch effect as explanation for fetal bacteria. *Microbiome*. 2021;9(1). doi:10.1186/S40168-020-00948-0
  19. Kuperman AA, Zimmerman A, Hamadia S. Deep microbial analysis of multiple placentas shows no evidence for a placental microbiome. *BJOG*. 2020;127(2):159-169. doi:10.1111/1471-0528.15896
  20. Koren N, Zubeidat K, Saba Y. Maturation of the neonatal oral mucosa involves unique epithelium-microbiota interactions. *Cell Host Microbe*. 2021;29(2):197-209.e5. doi:10.1016/J.CHOM.2020.12.006
  21. Al Nabhani Z, Eberl G. Imprinting of the immune system by the microbiota early in life. *Mucosal Immunol*. 2020;13(2):183-189. doi:10.1038/S41385-020-0257-Y
  22. Hornef MW, Torow N. ‘Layered immunity’ and the ‘neonatal window of opportunity’ – timed succession of non-redundant phases to establish mucosal host–microbial homeostasis after birth. *Immunology*. 2020;159(1):15-25. doi:10.1111/IMM.13149
  23. Ma J, Li Z, Zhang W. Comparison of gut microbiota in exclusively breast-fed and formula-fed babies: a study of 91 term infants. *Sci Rep*. 2020;10(1). doi:10.1038/S41598-020-72635-X
  24. Fragkou PC, Karaviti D, Zemlin M, Skevaki C. Impact of Early Life Nutrition on Children’s Immune System and Noncommunicable Diseases Through Its Effects on the Bacterial Microbiome, Virome and Mycobiome. *Front Immunol*. 2021;12. doi:10.3389/FIMMU.2021.644269/FULL

25. Martens EC, Neumann M, Desai MS. Interactions of commensal and pathogenic microorganisms with the intestinal mucosal barrier. *Nat Rev Microbiol.* 2018;16(8):457-470. doi:10.1038/S41579-018-0036-X
26. Cryan JF, O’Riordan KJ, Sandhu K, Peterson V, Dinan TG. The gut microbiome in neurological disorders. *Lancet Neurol.* 2020;19(2):179-194. doi:10.1016/S1474-4422(19)30356-4
27. Ho NT, Li F, Lee-Sarwar KA. Meta-analysis of effects of exclusive breastfeeding on infant gut microbiota across populations. *Nat Commun.* 2018;9(1). doi:10.1038/S41467-018-06473-X
28. Al Nabhani Z, Dulauroy S, Marques R. A Weaning Reaction to Microbiota Is Required for Resistance to Immunopathologies in the Adult. *Immunity.* 2019;50(5):1276-1288.e5. doi:10.1016/J.IMMUNI.2019.02.014
29. García-Mantrana I, Selma-Royo M, González S, Parra-Llorca A, Martínez-Costa C, Collado MC. Distinct maternal microbiota clusters are associated with diet during pregnancy: impact on neonatal microbiota and infant growth during the first 18 months of life. *Gut Microbes.* 2020;11(4):962-978. doi:10.1080/19490976.2020.1730294
30. Dierikx TH, Visser DH, Benninga MA. The influence of prenatal and intrapartum antibiotics on intestinal microbiota colonisation in infants: A systematic review. *Journal of Infection.* 2020;81(2):190-204. doi:10.1016/J.JINF.2020.05.002
31. Yan D, Ye S, He Y. Fatty acids and lipid mediators in inflammatory bowel disease: from mechanism to treatment. *Front Immunol.* 2023;14. doi:10.3389/FIMMU.2023.1286667/FULL
32. Lokossou GAG, Kouakanou L, Schumacher A, Zenclussen AC. Human Breast Milk: From Food to Active Immune Response With Disease Protection in Infants and Mothers. *Front Immunol.* 2022;13. doi:10.3389/FIMMU.2022.849012/FULL
33. Di Simone N, Santamaria Ortiz A, Specchia M. Recent Insights on the Maternal Microbiota: Impact on Pregnancy Outcomes. *Front Immunol.* 2020;11. doi:10.3389/FIMMU.2020.528202/FULL
34. Kalbermatter C, Fernandez Trigo N, Christensen S, Ganai-Vonarburg SC. Maternal Microbiota, Early Life Colonization and Breast Milk Drive Immune Development in the Newborn. *Front Immunol.* 2021;12:683022. doi:10.3389/FIMMU.2021.683022/BIBTEX
35. Mackie J, Suan D, McNaughton P. Functional validation of a novel STAT3 ‘variant of unknown significance’ identifies a new case of STAT3 GOF syndrome and reveals broad immune cell defects. *Clin Exp Immunol.* 2025;219(1). doi:10.1093/CEI/UXAF005
36. Moundir A, Aissaoui O, Akhrichi N. Application of Whole-Exome Sequencing to Predict Inborn Errors of Immunity in Pediatric Severe Infections and Sepsis. *Clin Exp Immunol.* Published online February 7, 2025. doi:10.1093/CEI/UXAF007
37. Nyangahu DD, Jaspan HB. Influence of maternal microbiota during pregnancy on infant immunity. *Clin Exp Immunol.* 2019;198(1):47-56. doi:10.1111/CEI.13331
38. Bokulich NA, Chung J, Battaglia T. Antibiotics, birth mode, and diet shape microbiome maturation during early life. *Sci Transl Med.* 2016;8(343). doi:10.1126/SCITRANSLMED.AAD7121



39. Korpela K, Zijlmans MAC, Kuitunen M. Childhood BMI in relation to microbiota in infancy and lifetime antibiotic use. *Microbiome*. 2017;5(1). doi:10.1186/S40168-017-0245-Y
40. Mulder B, Pouwels KB, Schuiling-Veninga CCM. Antibiotic use during pregnancy and asthma in preschool children: the influence of confounding. *Clinical and Experimental Allergy*. 2016;46(9):1214-1226. doi:10.1111/CEA.12756

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