

The following studies explore emerging and growing evidence that genetics, prenatal environments, delivery modes and early postnatal environments including feeding method can affect the infant microbiome, with significant implications for the infant immune system and both short- and long-term health outcomes.

## Frequent use of antimicrobial drugs in early life shifts bacterial profiles in saliva

The Finnish Health in Teens study (Fin-HIT) is a cohort study including over 11,000 Finnish adolescents. In the most recent Fin-HIT study, researchers tried to find the associations of lifelong AMs use with saliva microbiota diversity and composition in preadolescents. They used data from 808 randomly selected children in the Fin-HIT cohort with objective register data on AM purchases from the Social Insurance Institution of Finland (KELA). Results found that on average, the children had 7.4 AM purchases during their lifespan until on average 12 years. The four most commonly used AMs were amoxicillin (43.7 %), azithromycin (24.9 %), amoxicillin-clavulanate (18.7 %) and phenoxymethylpenicillin (6.8 %). The strongest associations were presented with azithromycin that is used for example to middle ear infections, strep throat and pneumonia.

University of Helsinki, ScienceDaily 24<sup>th</sup> August 2020  
"Frequent use of antimicrobial drugs in early life shifts bacterial profiles in saliva"



## Composition and variation of the human milk microbiota are influenced by maternal and early-life factors

This study of 393 mother-infant dyads from the CHILD cohort explored the factors affecting the complex community of bacteria in breastmilk, which may in turn help seed the infant gut microbiota.

Researchers found that milk microbiota composition and diversity were associated with maternal factors (BMI, parity, and mode of delivery), breastfeeding practices, and other milk components in a sex-specific manner.

Causal modelling identified mode of breastfeeding as a key determinant of milk microbiota composition. Specifically, providing pumped breastmilk was consistently associated with multiple microbiota parameters including enrichment of potential pathogens and depletion of bifidobacteria.

The findings also support the hypothesis that infant oral cavity, rather than mother's own gut microbiome, impacts the milk microbiota.

Moossavi, S. Sepehri, S. Robertson, B, et al (2019)  
"Composition and Variation of the Human Milk Microbiota are Influenced by Maternal and Early-Life Factors"



[Read a summary of this study \(Gut Microbiota for Health, by ESNM\)](#)



## Infant Feeding and the Developmental Origins of Chronic Disease in the CHILD Cohort: Role of Human Milk Bioactives and Gut Microbiota

This article provides a useful summary of recent studies exploring potential links between early life exposures and the development of chronic diseases such as allergies, asthma and obesity.

In particular, the studies highlight the potential for infant feeding method to impact the infant gut microbiota and so later health.

Summaries of some of the studies featured in this article can be found on this page, as well as on our [asthma](#) and [overweight/obesity](#) research pages.

Azad, M, (2019) "Infant Feeding and the Developmental Origins of Chronic Disease in the CHILD Cohort: Role of Human Milk Bioactives and Gut Microbiota"



## Impact of early events and lifestyle on the gut microbiota and metabolic phenotypes in young school-age children

This study of infants from the KOALA Birth Cohort found that breastfeeding duration in early life and pre-school dietary lifestyle correlated with the composition and functional competences of the gut microbiota in children at school age.

The researchers' findings also suggest that distinct metabolic responses to dietary lifestyle are strongly governed by the composition and functional potentials of the gut microbiota, implying that stratification of children according to gut microbiota enterotypes may well be included in future investigations on the relationship between dietary intake and metabolic health in children.

Zhong, H, Penders, J, Shi, Z et al (2019) "Impact of early events and lifestyle on the gut microbiota and metabolic phenotypes in young school-age children"



Early life gut microbiome as an obesity and type 1 diabetes predictor

This article highlights three studies recently published which explore the impact of the gut microbiome on health.

One study (Stanislawski et al) found an association between early life gut microbiota, particularly at two years of age, and BMI at age 12 in a Norwegian prospective cohort.

The other two studies were part of The Environmental Determinants of Diabetes in the Young (TEDDY) study, exploring the development of type 1 diabetes (T1D).

One study (Stewart et al) found that receipt of breast milk, either exclusive or partial, was the most significant factor associated with the microbiome structure and that birth mode was also significantly associated with the microbiome during the developmental phase.

The researchers found subtle associations between microbial taxonomy and the development of islet autoimmunity or T1D.

The other study (Vatanen et al) found that children who developed T1D later in childhood had different microbial features than those who didn't develop it; for example the gut microbiome of children who did not develop T1D later in childhood contained more genes related to fermentation and short-chain fatty acid production, whose protective role in metabolic conditions have been shown previously.

The findings suggest that the early life gut microbiome may help identify children who are at risk of obesity or T1D and may support prevention efforts.

Andreu Prados "Early life gut microbiome as an obesity and type 1 diabetes predictor"



Stanislawski, M, Dabelea, D Wagner, B, et al (2018) "Gut Microbiota in the First 2 Years of Life and the Association with Body Mass Index at Age 12 in a Norwegian Birth Cohort"



Stewart, C, Ajami, N, et al (2018) "Temporal development of the gut microbiome in early childhood from the TEDDY study"



Vatanen, T, Franzosa, E, Schwager, R, et al (2018) "The human gut microbiome in early-onset type 1 diabetes from the TEDDY study"



## Meta-analysis of effects of exclusive breastfeeding on infant gut microbiota across populations

This study performed a meta-analysis of seven microbiome studies (1825 stool samples from 684 infants) to compare the gut microbiota of exclusively breastfed (EBF) and non-EBF infants across populations.

The authors found that compared with EBF infants, non-EBF infants had increased microbial diversity and microbiota age, and altered microbial composition and functions.

EBF was found to have a protective effect on the infant gut microbiota during diarrheal episodes, and gut microbiota differences between EBF and non-EBF infants persisted after 6 months.

The researchers conclude that the findings help explain some mechanisms of short and long-term benefits of exclusive breastfeeding.

Nahn T. Ho, Fan Li et al (2018) "Meta-analysis of effects of exclusive breastfeeding on infant gut microbiota across populations"



## Association of exposure to formula in the hospital and subsequent infant feeding practices with gut microbiota and risk of overweight in the first year of life

This study found that among 1087 infants from the Canadian Healthy Infant Longitudinal Development (CHILD) cohort, earlier cessation of breastfeeding and supplementation with formula (more so than complementary foods) were associated with a dose-dependent increase in risk of overweight by age 12 months; this association was partially explained by specific gut microbiota features at 3 to 4 months.

Subtle but significant microbiota differences were observed after brief exposure to formula limited to the birth hospital stay, but these differences were not associated with overweight.

Forbes, J, Azad, B, et al (2018) "Association to Exposure to Formula in the Hospital and Subsequent Infant Feeding Practices with Gut Microbiota and Risk of Overweight in the First Year of Life"



### A casual mechanism for childhood acute lymphoblastic leukaemia

This review explores the multifactorial causation of childhood acute lymphoblastic leukaemia (ALL). It argues that there are three stages to the development of the disease: an initial genetic mutation that takes place in the womb; a lack of exposure to microbes in the first year of life; a childhood infection which can cause immune system malfunction.

The study highlights the important role that microbes play in determining health outcomes, as well as the value of breastfeeding in supporting the development of these microbes in an infant's gut.

Greaves, Mel, (2018) "A casual mechanism for childhood acute lymphoblastic leukaemia"



Further analysis of this review (BBC News)



### Association between breast milk bacterial communities and establishment and development of the infant gut microbiome

The establishment of the infant microbiome has lifelong implications on health and immunity, with gut microbiota of breastfed compared with non-breastfed individuals differ during infancy as well as into adulthood. Breastmilk contains a diverse population of bacteria, but little is known about the vertical transfer of bacteria from mother to infant by breastfeeding. In this 12-month longitudinal study of 107 healthy mother-infant pairs, researchers explored whether maternal breastmilk and areolar skin bacterial communities transferred to the infant gut. They found that breastfed infants received 27.7% of their gut bacteria from breast milk and 10.4% from areolar skin during the first month of life. They concluded that microbes in mother's breastmilk seed the infant gut, including those associated with beneficial effects, underscoring the importance of breastfeeding in the maturation of the infant gut microbiome.

Pannaraj, P.S. et al (2017) "Association between Breast Milk Bacterial Communities and Establishment and Development of the Infant Gut Microbiome"



## The microbiome in early life: implications for health outcomes

Recent studies have characterised how host genetics, prenatal environment and delivery mode can shape the newborn microbiome at birth.

Following this, postnatal factors, such as antibiotic treatment, diet or environmental exposure, further modulate the development of the infant's microbiome and immune system, and exposure to a variety of microbial organisms during early life has long been hypothesized to exert a protective effect in the newborn.

Furthermore, epidemiological studies have shown that factors that alter bacterial communities in infants during childhood increase the risk for several diseases, highlighting the importance of understanding early-life microbiome composition.

This review describes how prenatal and postnatal factors shape the development of both the microbiome and the immune system.

Tamburini, S, et al (2016) "The microbiome in early life: implications for health outcomes"



## Childbirth and consequent atopic disease: emerging evidence on epigenetic effects based on the hygiene and EPIIC hypotheses

This paper examines the emerging evidence that certain intrapartum and early neonatal interventions might affect the neonatal immune response in the longer term, and perhaps trans-generationally.

It discusses the two leading theories in this area: the hygiene hypothesis, and the EPIIC hypothesis.

The hygiene hypothesis proposes that in-utero, and in the first hours, weeks or months of life, the baby needs to gather a community of pre-existing microbes that come from the mother, as well as being exposed to bacteria from the surrounding environment, in order to protect against atopic and immunological diseases.

The EPIIC hypothesis, in contrast, suggests that when labour and birth occur primarily without intervention (when the process proceeds physiologically) a healthy positive form of stress (eustress) is exerted on the fetus which programmes immune responses, genes responsible for weight regulation, and specific tumor-suppressor genes.

The authors suggest drawing on both theories to help explain recent rises in the incidence of atopic and autoimmune disease.

Dahlen, HG, et al (2016) "Childbirth and consequent atopic disease: emerging evidence on epigenetic effects based on the hygiene and EPIIC hypotheses"



## The infant microbiome development: mom matters

In this evidence review, the authors argue that the infant microbiome plays an essential role in human health and its assembly is determined by maternal-offspring exchanges of microbiota.

This process is affected by several practices, including Caesarean section (C-section), perinatal antibiotics, and formula feeding, which have been linked to increased risks of metabolic and immune diseases.

The authors review recent knowledge about the impacts on infant microbiome assembly, discuss preventive and restorative strategies to ameliorate the effects of these impacts, and highlight where research is needed to advance this field and improve the health of future generations.

Mueller, NT, et al (2014) Trends in Molecular Medicine "The infant microbiome development: mom matters"



## Caesarean Section and Chronic Immune Disorders

In this study, mature children born by caesarean delivery were analysed for risk of hospital contact for chronic immune diseases recorded in the Danish national registries in the 35-year period 1977–2012.

Two million term children participated in the primary analysis.

Researchers found that children delivered by caesarean delivery had significantly increased risk of asthma, systemic connective tissue disorders, juvenile arthritis, inflammatory bowel disease, immune deficiencies, and leukaemia.

No associations were found between caesarean delivery and type 1 diabetes, psoriasis, or celiac disease.

Sevelsted, A, et al (2014) "Cesarean Section and Chronic Immune Disorders"



## Epigenetic effects of human breast milk

This paper suggests that although the different epigenetic mechanisms involved remain unclear, the benefits of breastfeeding against necrotising enterocolitis (NEC), infectious diseases, obesity and related-disorders, and cancer might be partly explained by the epigenetic model.

By modulating gene expression without changing the nucleotide sequence of DNA, breast milk might positively modify the phenotype and the outcome even if there is a genetic predisposition for the development of diseases.

Verduci, E, et al (2014) "Epigenetic Effects of Human Breast Milk"



## Natural Childbirth and Breastfeeding as Preventive Measures of Immune- Microbiome Dysbiosis and Misregulated Inflammation

This review argues that whilst technological advances in the management of pregnancy, childbirth and infant development have helped reduce the burden of some childhood illnesses, they have also undermined the microbial-rich experiences of natural childbirth and breastfeeding, producing serious, unanticipated consequences for today's children: an increased likelihood for human-microbiome incompleteness, lifelong immune dysfunction, and inflammation-promoted chronic disease.

This review will examine recent evidence suggesting that a more effective blending of ancient practices and remedies with modern technology and medical knowledge could help to restore the human-microbiome super organism to its historic status, improve paediatric immune homeostasis and reduce risk of later-life chronic diseases.

Dietert, RR (2013) Journal of Infectious Diseases& Preventive Medicine "Natural Childbirth and Breastfeeding as Preventive Measures of Immune-Microbiome Dysbiosis and Misregulated Inflammation"





## An overview of epigenetics in nursing

Epigenetic changes to the genome are biochemical alterations to the DNA that do not change an individual's genome but do change and influence gene expression.

This article discusses current epigenetic nursing research, provides an overview of how epigenetic research relates to nursing practice, makes recommendations, and provides epigenetic online resources for nursing research.

An overview of major epigenetic studies in nursing (specific to childbirth studies, preeclampsia, metabolic syndrome, immunotherapy cancer, and pain) is provided, with recommendations on next steps.

Clark, A, et al (2013) The Nursing Clinics of North America "An overview of epigenetics in nursing"



## The human milk microbiome changes over lactation and is shaped by maternal weight and mode of delivery

This study found that maternal weight and mode of delivery impacted the human milk microbiome. Milk from obese mothers tended to contain a different and less diverse bacterial community compared with milk from normal-weight mothers.

Milk samples from elective but not from nonelective mothers who underwent caesarean delivery contained a different bacterial community than did milk samples from individuals giving birth by vaginal delivery, suggesting that it is not the operation per se but rather the absence of physiological stress or hormonal signals that could influence the microbial transmission process to milk.

The findings emphasise the necessity to better understand the role that the microbiome could play for human health.

Cabrera-Rubio, R, et al (2012) American Journal of Clinical Nutrition "The human milk microbiome changes over lactation and is shaped by maternal weight and mode of delivery"



## Epigenetic changes in early life and future risk of obesity

This study reviews evidence for the impact of fetal and early postnatal environments on the risk of developing obesity in later life, with a focus on how particular environments can alter epigenetic regulation of specific genes.

The researchers suggest that understanding the role of epigenetics in risk of obesity opens the possibility of new interventions to modify long-term obesity risk and combat the rapid rise in obesity that has been occurring over the last two decades.

Lillicrop, KA, and Burdge, GC (2011) International Journal of Obesity "Epigenetic changes in early life and future risk of obesity"

