Relationships Between Perinatal Interventions, Maternal-Infant Microbiomes, and Neonatal Outcomes

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KEYWORDS

• Microbiome • Perinatal • Pregnancy • Preterm birth • Prematurity • Neonate

KEY POINTS

- Premature neonates have a delay in the colonization of "healthy" commensal bacteria and a propensity toward harboring pathogenic bacteria, an attribute that may be a key etiology for the premature neonate's increased susceptibility to develop necrotizing enterocolitis or other infections.
- Mode of delivery does not seem to substantially alter the infant microbiome. Instead, only formula feeding and maternal diet have lasting impacts on the infant microbiome.
- The fetus does not lie in a sterile environment. It is likely that in utero exposure to microbes and/or a microbe's free DNA leads to fetal immune system priming and regulation.
- The maternal diet is a potent modifier of both the mother's and the infant's microbiome. Further studies are needed to evaluate the effects of the maternal diet on the breast milk microbiome.
- Dysbiosis of the maternal microbiome is currently a leading hypothesis underlying the etiology of preterm birth. Therefore, further studies evaluating the microbiome can help elucidate potential treatments for preventing preterm birth—the leading cause of death throughout the world in children under 5 years of age.

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INTRODUCTION

The human body is host to a diverse array of largely commensal bacteria, which collectively across all body niches comprise an individual's personal microbiome. The Human Microbiome Project, completed in 2012, sought to define reference "healthy" microbiomes by evaluating and characterizing the microbiome across multiple body sites in healthy individuals of different races and ethnicities in the United States. Overall, this robust, multicenter study found that niche specificity, bacterial diversity, and microbial gene carriage patterns far surpassed what was previously thought.[1–4] Importantly, commensal microbiota are more than simple bystanders because their presence and unique metabolic processes are essential components of our own physiology. Moreover, it is thought that the nature, state, and composition of the microbiome are related to (and likely contribute to) the development of several common human diseases. Dysbiosis of the human microbiome, defined as an aberrant microbial community, has been associated with the development of diabetes,[5–8] inflammatory bowel disease,[9–13] obesity,[14,15] metabolic syndrome,[16] and autoimmune disorders,[15,17,18–29] although causation has yet to be established.

In keeping with the developmental origins of health and disease hypothesis,[30–37] it is thought that the role of the microbiome in disease pathogenesis likely initiates in early life during key developmental windows, predisposing an individual to develop disease later in life when and if exposed to the right environmental triggers. Mice raised in the relative or complete absence of bacteria (gnotobiotic and germ-free mice) have immune deficits that cannot be restored completely unless the infant and mother are exposed to bacteria in pregnancy and early life.[38,39] For these reasons, understanding when and how the neonatal microbiome is first established, how it develops in the immediate postnatal period, and what external factors (eg, mode of delivery and breastfeeding) modify its trajectory has been a recent focus of the field.

Recent literature surrounding the perinatal microbiome has seen increased attention and focus. This article seeks to consolidate and evaluate the medical literature assessing common perinatal interventions, their effects on the infant microbiome, and their potential benefit to neonatal outcomes. First, pregnancy and the potential contribution of the maternal microbiome to preterm risk as well as the neonate's microbiome are discussed. Second, common perinatal interventions are explored, such as intrapartum antibiotic prophylaxis, mode of delivery, timing of delivery (premature vs term), hospitalization, and use of probiotics in both the mother and neonate. Finally, breastfeeding versus formula feeding is discussed and the impact each may have on neonatal outcomes.

PERINATAL AND POSTNATAL INTERVENTIONS AND THEIR IMPACT ON THE NEONATAL MICROBIOME

Although many perinatal interventions occur daily among the more than 4 million US births annually, including the use of probiotics or intrapartum antibiotic prophylaxis for group B streptococcus, and may seem relatively benign, the broad-reaching and longer-term impacts are unknown (**Fig. 1**). By contrast, broad-spectrum microbial interventions or manipulations have been studied a bit deeper and there is a bit more known about their impact on microbial communities, their structure, and their function. This article discusses the impact of preterm birth, common perinatal interventions, their influence on the fetal and neonatal microbiome, and the potential short-term and long-term neonatal outcomes.