Probiotic Intervention Through the Pregnant and Breastfeeding Mother to Reduce Disease Risk in the Child

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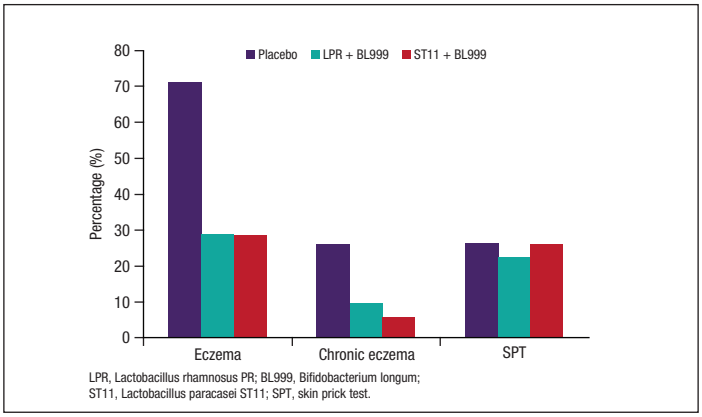
The incidence of infectious diseases has declined drastically since the 1950s, yet the incidence of chronic, non-communicable diseases has been steadily increasing.[1] Increased risk of non-communicable diseases is associated with disturbances in microbial contact and gut microbiota composition during infancy.[2-5] The mode of delivery (ie, vaginal birth or cesarean delivery) can greatly impact the initial microbiota in newborns.[6] Cesarean deliveries are associated with reduced gut microbiota diversity and increased risk of many chronic immune disorders (eg, asthma, inflammatory bowel diseases) later in life.[7-9] Breastfeeding is also an important modulator of the gut microbiome and is associated with reduced risk of disease. Human milk contains factors (eg, human milk oligosaccharides) that promote the growth of beneficial bacteria and may also be a source of bacteria for the developing gut.[10] The microbial composition of breast milk has been shown to vary with the mode of delivery and can change over the course of lactation.[11] Thus, modulation of early microbial contact through avoidance of unnecessary cesarean sections, promotion of breastfeeding, and prudent use of antibiotics may improve health outcomes. Other interventions, such as vaginal seeding after cesarean delivery and the use of prebiotics and probiotics, have also been investigated as a means to influence early microbial contact and to reduce disease risk.

Probiotics are defined as "live micro-organisms that, when administered in adequate amounts, confer a health benefit on the host."[12] Prenatal probiotic administration to high-risk pregnant women 2 to 4 weeks before delivery and 6 months postnatally to their infants has been shown to significantly decrease the risk of atopic eczema during the first 7 years of life.[13,14] Findings from a separate study demonstrated that probiotic supplementation exclusively to the mother (ie, the infants did not receive probiotics) during the last 2 months of pregnancy and the first 2 months of breastfeeding was also effective in reducing the risk of eczema in high-risk infants during the first 2 years of life **(Figure 1)**.[15]

Figure 1. Maternal probiotic supplementation during pregnancy and breastfeeding reduces the risk of developing eczema in high-risk infants.[15]



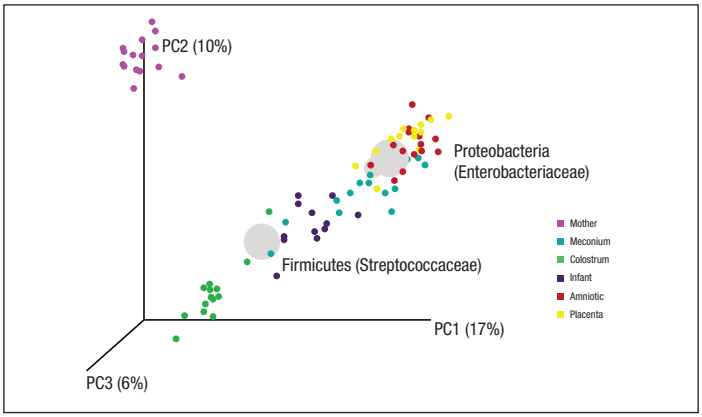
LPR, Lactobacillus rhamnosus PR; BL999, Bifidobacterium longum; ST11, Lactobacillus paracasei ST11; SPT, skin prick test.

Probiotic supplementation in pregnant and breastfeeding mothers may result in the transfer of probiotic bacteria to the infant and/or increases in gut microbiota diversity; however, recent data suggest maternal probiotic supplementation does not alter the infant microbiota.[16] The preventive mechanism of probiotic intervention in the mother may be associated with increases in immunomodulatory factors (eg, cytokines, growth factors) found in breast milk. Higher concentrations of transforming growth factor β2 (TGF-β2) have been reported in the breast milk of mothers receiving probiotics than in the breast milk of mothers receiving placebo.[13] Furthermore, TGF-β2 has been shown to attenuate interleukin 1β-induced production of proinflammatory cytokines in immature human intestinal epithelial cells.[17]

Probiotic supplementation during pregnancy may modulate prenatal microbial contact and fetal immune physiology. Microbes have been detected in healthy human placenta, amniotic fluid, and meconium.[18,19] A recent study characterizing these microbial populations demonstrated that the meconium microbiota share features with the microbiota of the placenta and amniotic fluid, suggesting the initial inoculum for gut colonization during fetal development may originate from the placenta and amniotic fluid **(Figure 2)**.[20]

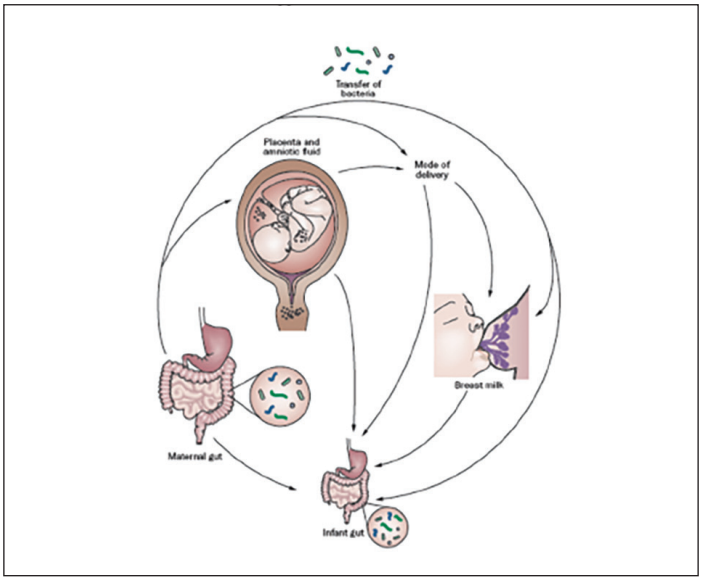
Consistent with this, probiotic intervention during the last 2 weeks of pregnancy was associated with changes in innate immune gene expression profiles in the placenta and fetal gut.[21]

Figure 2. Principal component analysis of different microbial communities in the mother and infant.[20]



Together, these findings suggest early microbial contact likely begins in utero and can be affected by various factors, such as mode of delivery and breastfeeding **(Figure 3)**.[22] Probiotic intervention during pregnancy and breastfeeding is associated with lower risk of disease, which may be due to enhanced protective effects of breast milk and modulation of prenatal microbial contact.

Figure 3. Microbial programming of the infant gut microbiota.[22]



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