# Keynote Speaker

## Signaling Between Mother and Infant During Lactation: Evolutionary, Anthropologic, Biologic, and Practical Considerations

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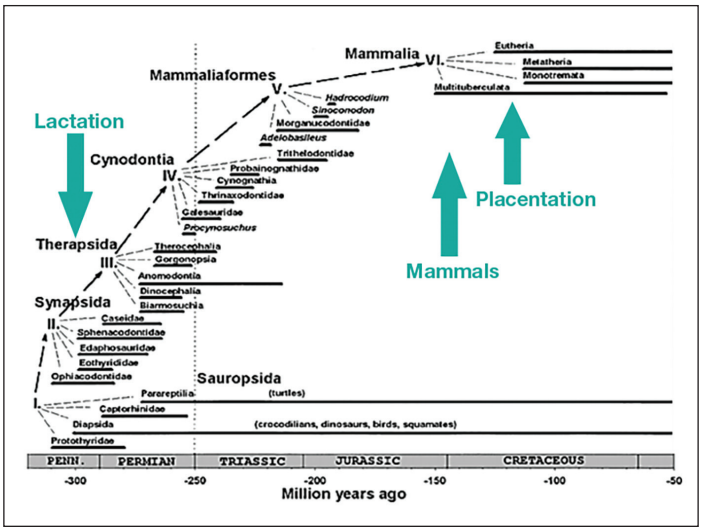
Breastfeeding has typically been considered as a one-way process in which the mother provides all the nutrition the infant requires. This "medical" perspective of breastfeeding has resulted in a prescriptive approach to breastfeeding recommendations based on nutritional requirements and evidence for health effects. However, when considering lactation from a broader evolutionary perspective, milk can be regarded as a "signal" between the mother and infant.

### Evolution of Lactation

Lactation is an ancient process that probably originated approximately 310 million years ago, long before the emergence of mammals and placentation **(Figure 1)**.[1,2] Mammary glands, which are unique to mammals, most likely evolved from apocrine glands but have acquired many unique features, such as repeated cycles of proliferation and secretion followed by apoptosis, secretion of a variety of products, and greater hormonal control. In addition to their original role in providing moisture and immune components to eggs, mammary glands subsequently developed a role in providing nutrients. The nutritional role of lactation conferred several advantages, including the ability to provide nutrition distant from a food source, a reduction in egg/yolk size, and the maturation of offspring before they required features needed to eat specialized diets. Many nutritional components in milk seem to have had an immune origin. For example, α-lactalbumin probably evolved from lysozyme, and many proteins found in the milk fat globule membrane (MFGM) were originally immune components. Milk and mammary genes are more highly conserved than other genes; the most conserved genes are required for milk secretion (eg, MFGM), while the most divergent genes tend to have nutritional or immunologic functions.[3]

**Figure 1. Evolution of lactation.[1]**




The production of milk enabled mammals to evolve a wide range of developmental and reproductive strategies. Smaller mammals typically produce energy-dense milk in order to meet high metabolic demands with low gastric capacity, while larger mammals tend to have more dilute milk due to greater storage capacity and maternal fat reserves. Primates produce milk that is low in fat and protein and have longer periods of lactation to support slow-growing offspring that are dependent on their parents; this spreads out the energy cost of investment for the mother, but also creates a source of conflict between the mother and infant, since lactation is energetically expensive.[4] The mother needs to invest in all her offspring and benefits from

early weaning and the next pregnancy, while the infant benefits from longer breastfeeding. Primate lactation also tends to rely more on learned behaviors rather than instinct and is therefore associated with a high degree of flexibility, which allows for better adaptation to environmental conditions.[5] Humans produce milk with higher fat and lower protein concentrations than other primates and have shorter periods of lactation with shorter intervals between births.[6] Humans also have a complementary feeding period in which breast milk is supplemented with other foods. Complementary feeding is flexible depending on the environment and may allow the mother to shorten the duration of lactation and regain fertility sooner. There is a greater reliance on learning and influence of culture in human lactation compared with other primates; however, many mothers do not experience learning opportunities in early life, which may explain why mothers may not follow breastfeeding recommendations.

**Signaling Between Mother and Infant During Lactation**

Lactation allows for greater and extended contact between the mother and infant and presents a wide range of signaling opportunities via milk content, volume, and behavior. There are numerous factors that could act as potential signaling components in milk, such as nutrients, growth factors, oligosaccharides, microRNAs, cells, and hormones. The hormones present in milk include those known to be important in energy homeostasis and appetite regulation (eg, leptin, ghrelin, adiponectin, insulin) and may influence infant behavior, appetite, growth, and body composition.[7] Hormones in human milk originate from the breast and maternal circulation and can reach the small intestine intact. However, limited data suggest milk hormones may influence offspring outcomes. Most studies are observational, and few studies measure infant outcomes beyond simple anthropometry. Furthermore, methodological issues (ie, milk sampling and processing, assays) make comparisons difficult. Stem cells found in breast milk are another potential candidate for signaling between the infant and mother. Breast milk stem cells are pluripotent, and their gene expression is influenced by maternal and infant factors.[8] Data from animal studies suggest breast milk stem cells can graft onto and proliferate in different organs in the offspring[9,10]; however, further experimental studies in humans are needed to better define their potential role in maternal–infant signaling.

Breastfeeding can be viewed from an anthropologic perspective as a conflict between the mother and infant.[11] The mother influences lactation by controlling access to the breast, altering milk volume and nutritional content, and through the inclusion of non-nutritive factors (eg, hormones, cells). The infant also influences this process through vocalization, feeding demands, and non-nutritive suckling. Reducing tension within this conflict may benefit both parties and improve lactation outcomes. An ongoing randomized trial is currently assessing whether relaxation therapy in primiparous mothers can reduce stress, increase breastfeeding success, and improve infant outcomes.

In summary, lactation is an ancient process with many highly conserved aspects, suggesting fundamental importance (eg, MFGM). Each mammal has a lactation strategy suited for its environment and lifestyle, but there is also flexibility within populations and between mothers. Primate lactation relies less on instinct and more on learning, behavior, and culture, emphasizing the importance of early breastfeeding education. Conflict or tension between mother and infant may underlie some lactation problems; thinking more broadly from an anthropologic perspective may help to explain some of these problems and define solutions. A better understanding of maternal–infant signaling that shapes breastfeeding behavior may also help to improve outcomes. Experimental approaches using standardized protocols and a wider range of infant outcomes will help better define the complex inter-relationships between signaling factors.

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