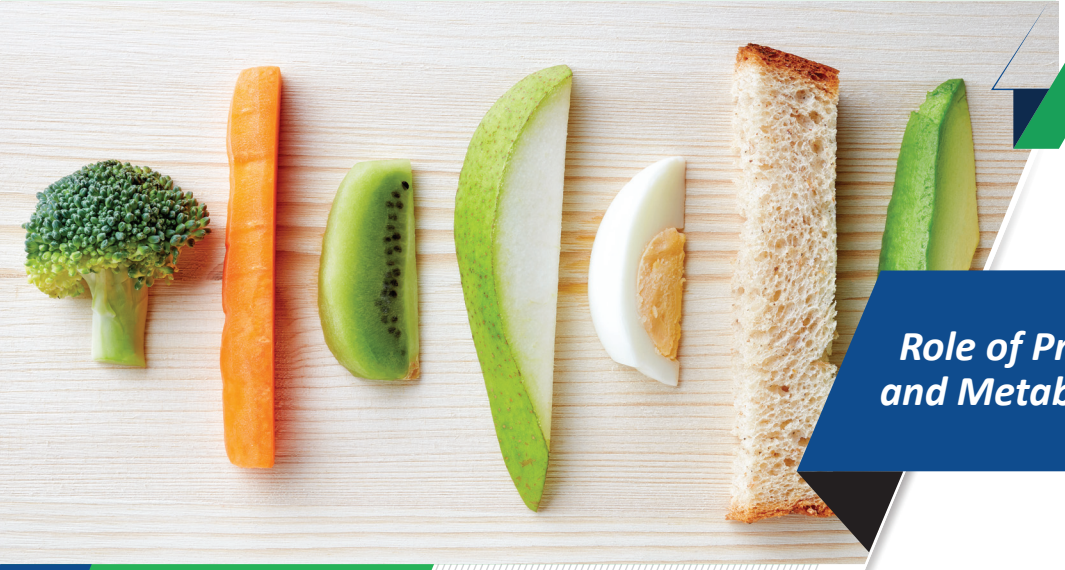

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# Role of Protein in Long-Term Health and Metabolic Programming

## Introduction

*Human milk is considered as the best source of infant nutrition. Evidence shows that mother's milk contains several bioactive agents that aid in healthy growth and development of the child. The composition of breast milk is such that it can prevent a growing epidemic, such as obesity, and other non-communicable diseases that are a result of poor early nutrition.*[1,2]

Breast milk is the gold standard for infant nutrition. Due to its unique composition, particularly the quality and quantity of proteins, breast milk is the ideal nutrition to support an infant's healthy growth and development. The first 1000 days of an infant's life is a critical window for development and nutrition during this period can influence metabolic programming. An excess of certain types of amino acids required in early nutrition, can cause early weight gain and can lead to obesity. Therefore, a right quality and quantity of proteins is important for an optimal development.

## Composition of Breast Milk and Healthy Growth Patterns

Breast milk is species-specific and considered to be superior to any other breast milk substitute, and hence is the ideal food within the first 6 months of an infant's life, ensuring optimal growth and development. Human milk is the most natural food and varies in composition from mother to mother, from feed to feed, and from day to day.[3] With respect to the composition, breast milk consists of 88% water, which is why the infant is exclusively breast-fed for the first 6 months. The total protein content in breast milk is 0.8–0.9 g/dL, which is less than a third of proteins when compared with other mammalian milk.[4] Moreover, human milk is whey-predominant, whereas cow's milk is casein-predominant (in human milk the whey/casein ratio is 72:28 and in cow's milk it is 18:82). In human whey proteins, all the essential amino acids are present, which provides adequate nutrition for the healthy growth and development of the infant. Besides, this breast milk also contains immunoprotective proteins, such as immunoglobulin A and lactoferrin, that protect the infant from infections.[2,5,6]

## Programming of Long-Term Health in The First 1000 Days

A growing body of evidence suggests that there exists a relationship between early nutrition and development of disease in later childhood and adult life. Some of the most powerful factors for the risk of obesity have been identified in the first 1000 days (from conception to 2 years of age) of the infant's life. This period is considered critical for both identifying and curbing certain factors that can lead to obesity later on. The first 1000 days have been divided into three main periods, which are prenatal (0–280 days), breast/formula-feeding phase (280 days to 6 months), and complementary and early-feeding phase (6 months to 2 years). In the prenatal period, maternal nutrition and weight gain contribute significantly to the child's risk for obesity. In the breast/formula-feeding stage, the protective role of breastfeeding is said to decrease the risk for obesity. However, cow-milk-based formula-fed infants are at a greater risk of developing diseases mainly because of the higher protein content in the formula which leads to increased levels of insulin-like growth factor-1 (IGF-1), resulting in increased adiposity. The decreased risk of obesity due to breast milk, however, is primarily attributed to lower energy and protein content than commercially available formulas. In the complementary feeding phase, the infant is fed milk other than human milk, such as cow's milk, in addition to solid foods. The increased protein in animal milk may lead to a rapid weight gain in late

childhood, and hence obesity in adult life. Therefore, long-term health is programmed in the first 1000 days of life, and the impact of early protein intake on growth and metabolic programming is becoming increasingly important.[7]

Risk factors for obesity in first 1000 days.

| Nutritional phase | Risk factor |
|---|---|
| Prenatal (0–280 days) | Higher maternal pre-pregnancy BMI<br>Excess maternal Gestational Weight Gain<br>Maternal Diabetes Mellitus (gestational or Type 1)<br>Genetic predisposition |
| Breast/Formula Feeding (280 days–6 months of age) | Formula feeding<br>• Accelerated growth curve<br>• High energy intake<br>• High protein content<br>• Low concentration of polyunsaturated fatty acids |
| Complementary and Early Diet (6 months–2 years of age) | Rapid weight gain<br>Early introduction of solids<br>High protein intake<br>Gut microbiome |

**Adapted from:** Mameli *et al*.[7]

## Impact of Being Overweight and Obese: Loss of Healthy Life Years

Incidences of childhood obesity are on the rise in recent times and have become a global issue. Obesity in childhood is associated with serious short- and long-term health impacts that affect the quality of life, performance, and lifespan of an individual. Several studies have shown that rapid weight gain in the first 2 years of life leads to obesity in late childhood and adulthood, thereby leading to loss of a healthy life in the critical growth periods.[8,9]

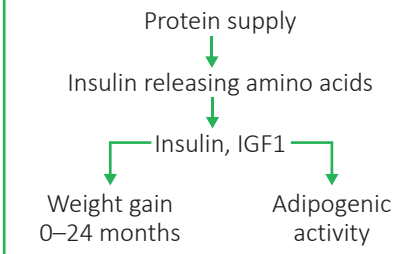
## Early Protein Hypothesis and Metabolic Dysprogramming

An increased intake of protein at an early age can lead to rise in insulin-like growth factor-1 or IGF-1 leading to increased adiposity. This phenomenon known as the early protein hypothesis is an important causative factor in childhood obesity.[7] Thus, early nutritional interventions are essential to avoid long-term consequences on health and prevent non-communicable diseases later on.[10] Modulating such metabolic factors both pre- and postnatally can instigate a lasting effect on the overall health and disease into adulthood and is termed as metabolic programming.[8] In this regard, breast milk, is thought to be protective and is deemed as a natural way of programming against excessive adiposity in adulthood.[11] On the other hand, increased protein intake with cow's milk leads to increased intake of amino acids like valine, leucine, iso-leucine, and threonine that stimulate IGF-1 which in turn can increase adipogenic activity.[12,9] This protective effect of breast-milk is due to the presence of hormones and adipokines that contribute to a self-regulation of an infant's appetite. The link between growth pathways and early protein hypothesis is moderated by both quantity and quality of protein intake.[9] The quantity of protein in breast milk is considerably lesser when compared to that in cow's milk.[13] On the other hand, increased protein intake with cow's milk leads to increased intake of amino acids like valine, leucine, iso-leucine, and threonine that stimulate IGF-1 which in turn can increase adipogenic activity.[12,9] The amino acid profile of the protein present in the breast milk determines its quality. Breast milk is predominantly rich in whey protein and alpha-lactalbumin constitutes a large part of the whey.[14] Alpha-lactalbumin has an exceptionally high concentration of tryptophan which regulates neurobehavioural effects such as appetite, satiation, mood, pain perception, and the sleep-wake rhythm.[15,16] On the other hand, cow's milk contains less of alpha-lactalbumin and majorly constitutes glycomacropeptide (GMP) which is significantly

rich in the branched chain amino acids (BCAAs) threonine but depleted in tryptophan.[15] Branched chain amino acids such as the leucine and threonine present in cow's milk is predominantly linked with early childhood obesity. Leucine is key in the activation of IGF-1 along with other insulin secreting hormones like valine and isoleucine.[8]

Thus, modifying the protein quality and quantity of infant formula to make it more similar to human milk, is considered beneficial in tackling obesity early in its course.[14,16] Evidence suggested that modified protein composition in infant formula with increased α-lactalbumin concentration with GMP that accounts for 15% or 10% of the protein and with a total protein content of <13 g/L was associated with growth patterns in infants that were similar to those of breastfed infants due to a reduction in plasma concentrations of insulinogenic amino acids.[17] The high plasma concentrations of all the essential amino acids in infants fed α-lactalbumin-rich formulas suggested that protein quantity can be reduced in a formula without compromising on the quality with use of high quality protein sources.[17] In line with the available evidence, the ESPGHAN in 2005 recommended that infant formula contain proteins in the range of 1.8–2.0 g/100 kcal, which is closer in range to human milk and also ensures minimum amino acid available for protein synthesis.[18]

**Early protein hypothesis.**




**Adapted from:** Koletzko, *et al*.[8]

## Conclusion

Obesity is on the rise globally, and early nutrition has been associated with late-childhood and adulthood obesity. Breast milk has emerged as protection against the risk for obesity when compared with cow-milk-based formulas, because of the low protein content in breast milk. Therefore, good early nutrition with protein intake according to metabolic requirements (as is available in breast milk) or formulas with protein and energy content close to that of breast milk can ensure long-term development and health.

**References**

1. Martin CR, Ling P-R, Blackburn GL. Review of infant feeding: Key features of breast milk and infant formula. *Nutrients*. 2016;8(5):279.
2. Feeding and Nutrition of Infants and Young Children. Available from: http://www.euro.who.int/__data/assets/pdf_file/0004/98302/WS_115_2000FE.pdf. Accessed on: 13 June 2018.
3. Motee A & Jeewon R. Importance of exclusive breast feeding and complementary feeding among infants. ***Curr Res Nutr Food Sci J***. 2014;2(2):56–72.
4. Nascimento and Issler H Breastfeeding: Making the difference in the development, health and nutrition of term and preterm newborns. *Rev Hosp Clin Fac Med S Paulo*. 2003;58(1):49–60.
5. Ballard O, Morrow AL. Human milk composition: Nutrients and bioactive factors. *Pediatr Clin North Am*. 2013;60(1):49–74.
6. Leung AKC, Sauve RS. Breast is best for babies. *J Nat Med Assoc*. 2005;97(7):1010–1019.
7. Mameli, Mazzantini, Vincenzo. Nutrition in the first 1000 days: The origin of childhood obesity. *Int J Environ Res Public Health*. 2016;13:838.
8. Koletzko B, von Kries R, Closa R, *et al*. Lower protein in infant formula is associated with lower weight up to age 2 y: A randomized clinical trial. *Am J Clin Nutr*. 2009;89(6):1836–1845.
9. Koletzko B, Demmelmair H, Grote V, *et al*. High protein intake in young children and increased weight gain and obesity risk. *Am J Clin Nutr*. 2016;103:303–304 .
10. Verduci E, Mariani B, Lassandro C, *et al*. Protein intake and nutritional programming: metabolic consequences. *Ital J Pediatr*. 2014, 40(Suppl 1):A49
11. Rigo J, Ziegler EE (eds). Protein and Energy Requirements in Infancy and Childhood. *Nestlé Nutr Workshop Ser Pediatr Program*, vol 58, pp 189–205.
12. Luque V, Closa-Monasterolo R, Escribano J, Ferré N. Early programming by protein intake: The effect of protein on adiposity development and the growth and functionality of vital organs. *Nutr Metab Insights*. 2015;8(Suppl 1):49–56.
13. Williams HH. Differences Between Cow's and Human Milk. *JAMA*. 1961;175(2):104–107.
14. Dutta S, Hazarika RD, Banerjee S, *et al*. Protein quality in early infancy and long-term health outcomes. *Clin Epidemiol Global Health*. 2017;5:101–106.
15. Heine WE. Qualitative Aspects of Protein in Human Milk and Formula: Amino Acid Pattern. *Nestle Nutrition Workshop Series*. 1994. Vol. 33.
16. Lien E, Davis A, Euler A. Infant formulas with increased concentrations of alpha-lactalbumin. *Am J Clin Nutr*. 2003;77(suppl):1555S–8S.
17. Sandström O1, Lönnerdal B, Graverholt G, *et al*. Effects of alpha-lactalbumin-enriched formula containing different concentrations of glycomacropeptide on infant nutrition. *Am J Clin Nutr*. 2008 Apr;87(4):921–928.
18. Koletzko B, Baker S, Cleghorn G, *et al*. Global Standard for the Composition of Infant Formula: Recommendations of an ESPGHAN Coordinated International Expert Group. *J Pediatr Gastroenterol Nutr*. 2005.

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