The Impact of Human Milk Feeding on Long-Term Risk of Obesity and Cardiovascular Disease

Atul Singhal^{1,2}

BYOND JUST MEETING NUTRITIONAL REQUIREMENTS, nutrition during infancy is linked to disease later in life, a concept known as “the developmental origins of health and disease.” As early as the 1930s, study in rodents demonstrated that early calorie restriction increased the life span by 35% and reduced the incidence of tumors, kidney disease, vascular calcification, and chronic pneumonia.¹ In the 1960s, studies in rats showed that early nutrition during the first 3 weeks had a life-long impact on body size; rats that received less milk during this time continued to weigh less throughout life compared with rats that received more milk.² Further evidence for nutritional programming came from studies in baboons, which showed that overfeeding during infancy increased the tendency for obesity in adulthood.³

One of the first studies to demonstrate nutritional programming in humans showed that rapid weight gain from as early as the first 6 weeks of life was associated with obesity at 8 years of age.⁴ Beginning in the late 1980s, observational studies linking low birth weight with later cardiovascular risk factors and diabetes shifted focus to nutrition during the fetal period, resulting in the “fetal origins of adult disease” hypothesis.⁵ Subsequent studies have suggested that, although a high-quality maternal diet can prevent infants born small for gestational age (SGA) and low birth weight, dietary supplementation during pregnancy may not affect the offspring’s risk of obesity and cardiovascular disease.^{6–9} Other studies suggest prepregnancy obesity and maternal weight gain are associated with obesity in the offspring; however, there has been no convincing evidence of a causal effect of these factors on offspring obesity.^{10–12}

There have been several systematic reviews supporting the positive effects of breastfeeding on cardiovascular risk factors, such as obesity and type 2 diabetes.^{13,14} Experimental trials in preterm infants assigned to donor human milk or formula demonstrated the beneficial effects of human milk on blood pressure, cholesterol, obesity, and insulin resistance.^{15–18} One possible explanation for the benefits of human milk on cardiovascular risk may be the slower growth of infants receiving breast milk versus those receiving formula (i.e., the growth acceleration hypothesis).¹⁹ Human milk has lower energy and protein content than formula, resulting in slower weight gain during infancy with human milk

versus formula. Faster infant growth has been associated with later obesity in many studies, including five randomized trials.¹⁹ A randomized trial of high nutrient intake in term SGA infants showed that infants fed enriched formula had significantly higher diastolic blood pressure and fat mass at 6–8 years compared with those fed standard formula.^{20,21} Similarly, a multicenter randomized trial by the European Childhood Obesity Group reported a significantly higher body mass index and a 2.4 times greater risk of becoming obese at 6 years of age in infants who had been fed a high-protein formula versus those fed a low-protein formula in infancy.²² It has been hypothesized that accelerated growth in infancy may result in hormonal changes that program a higher set point for appetite, leading to higher food intake throughout life.²³ Bottle-fed infants may be less likely to regulate milk intake or appetite later in infancy; infants receiving human milk from a bottle were 67% less likely to have a high satiety response.²⁴

In summary, there is strong evidence supporting the benefits of breastfeeding and human milk consumption during infancy for long-term cardiovascular health. These benefits may be related to the slower early growth of infants receiving human milk or lower-protein formulas versus those fed standard formulas. Preventative strategies, such as promoting breastfeeding, reducing the protein content of formula, avoiding overnutrition, and encouraging responsive bottle feeding (i.e., recognizing feeding cues), may help to slow the rate of weight gain in infancy and reduce the long-term burden of cardiovascular disease.

Disclosure Statement

No competing financial interests exist.

References

1. McCay CM. Is longevity compatible with optimum growth? *Science* 1933;77:410–411.
2. Widdowson EM, McCance RA. Some effects of accelerating growth. I. General somatic development. *Proc R Soc Lond B Biol Sci* 1960;152:188–206.
3. Lewis DS, Bertrand HA, McMahan CA, et al. Prewaning food intake influences the adiposity of young adult baboons. *J Clin Invest* 1986;78:899–905.

¹Institute of Child Health, University College London, London, United Kingdom.

²Great Ormond Street Hospital, London, United Kingdom.

4. Eid EE. Follow-up study of physical growth of children who had excessive weight gain in first six months of life. *Br Med J* 1970;2:74–76.
5. Barker DJ. Fetal origins of coronary heart disease. *BMJ* 1995;311:171–174.
6. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2015;CD004905.
7. Ota E, Hori H, Mori R, et al. Antenatal dietary education and supplementation to increase energy and protein intake. *Cochrane Database Syst Rev* 2015;CD000032.
8. Hawkesworth S, Walker CG, Sawo Y, et al. Nutritional supplementation during pregnancy and offspring cardiovascular disease risk in The Gambia. *Am J Clin Nutr* 2011;94:1853S–1860S.
9. Fall C. Maternal nutrition: effects on health in the next generation. *Indian J Med Res* 2009;130:593–599.
10. Patro B, Liber A, Zalewski B, et al. Maternal and paternal body mass index and offspring obesity: A systematic review. *Ann Nutr Metab* 2013;63:32–41.
11. Yu Z, Han S, Zhu J, et al. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: A systematic review and meta-analysis. *PLoS One* 2013;8:e61627.
12. Sharp GC, Lawlor DA, Richardson SS. It's the mother!: How assumptions about the causal primacy of maternal effects influence research on the developmental origins of health and disease. *Soc Sci Med* 2018;213:20–27.
13. Horta BL, Loret de Mola C, Victora CG. Long-term consequences of breastfeeding on cholesterol, obesity, systolic blood pressure and type 2 diabetes: A systematic review and meta-analysis. *Acta Paediatr* 2015;104:30–37.
14. Patro-Gofab B, Zalewski BM, Kołodziej M, et al. Nutritional interventions or exposures in infants and children aged up to three years and their effects on subsequent risk of overweight, obesity, and body fat: A systematic review of systematic reviews. *Obes Rev* 2016;17:1245–1257.
15. Singhal A, Cole TJ, Lucas A. Early nutrition in preterm infants and later blood pressure: Two cohorts after randomised trials. *Lancet* 2001;357:413–419.
16. Singhal A, Farooqi IS, O'Rahilly S, et al. Early nutrition and leptin concentrations in later life. *Am J Clin Nutr* 2002;75:993–999.
17. Singhal A, Fewtrell M, Cole TJ, et al. Low nutrient intake and early growth for later insulin resistance in adolescents born preterm. *Lancet* 2003;361:1089–1097.
18. Singhal A, Cole TJ, Fewtrell M, et al. Breastmilk feeding and the lipoprotein profile in adolescents born preterm. *Lancet* 2004;363:1571–1578.
19. Singhal A. Long-term adverse effects of early growth acceleration or catch-up growth. *Ann Nutr Metab* 2017;70:236–240.
20. Singhal A, Cole TJ, Fewtrell M, et al. Promotion of faster weight gain in infants born small for gestational age: Is there an adverse effect on later blood pressure? *Circulation* 2007;115:213–220.
21. Singhal A, Kennedy K, Lanigan J, et al. Nutrition in infancy and long-term risk of obesity: Evidence from 2 randomized controlled trials. *Am J Clin Nutr* 2010;92:1133–1144.
22. Weber M, Grote V, Closa-Monasterolo R, et al. Lower protein content in infant formula reduces BMI and obesity risk at school age: Follow-up of a randomized trial. *Am J Clin Nutr* 2014;99:1041–1051.
23. Widdowson EM, McCance RA. A review: New thoughts on growth. *Pediatr Res* 1975;9:154–156.
24. Disantis KI, Collins BN, Fisher JO, et al. Do infants fed directly from the breast have improved appetite regulation and slower growth during early childhood compared with infants fed from a bottle? *Int J Behav Nutr Phys Act* 2011;8:89.

Address correspondence to:
 Atul Singhal, MD, MRCP
 Institute of Child Health
 University College London
 WC1N 1EH London
 United Kingdom

E-mail: a.singhal@ucl.ac.uk