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Exclusively Breastfed Babies: Are They Getting Enough Iron?

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Editorial

An important question pertaining to the nutritional needs of human infants currently remains unanswered. Are exclusively breastfed infants, whose sole source of iron is breast milk, receiving an adequate amount of iron? The iron concentrations in the milk of other, non-human species are considerably higher than that of humans. The iron concentration in human colostrum is approximately 0.8 µg/ml, while that in mature human milk is 0.2-0.4 µg/ml. In contrast, the iron concentration in mature rat milk is 5-10 µg/ml, a value that is roughly 25 times higher [1]. Although iron concentration in human milk is low, it is seemingly independent of the mother's iron status. It therefore cannot be increased through alterations in the maternal diet, or by use of supplementation [2]. Further, studies have shown that the iron concentration in mother's milk is fairly similar in those with high and low intakes of iron [3,4]. There is still much controversy, as well as a lack of agreement among the scientific community with regards to what should be recommended for infants when it comes to iron. Do they need more iron, possibly provided through supplementation? Are they obtaining sufficient amounts of iron through the natural process of breast feeding? This article aims to show both the concerns and the relevant support for each side of this argument.

Iron deficiency anemia (IDA) is a common cause of anemia in infants. Early iron deficiency is associated with later neurodevelopmental impairment [5]. A longitudinal study in Costa Rica assessed changes in cognitive functioning following iron deficiency in infancy. This was done by scheduling 4 follow-up visits at the ages of 5, 11-14, 15-18, and 19 years old. The results showed that iron deficient infants had lower cognition scores compared to the control group, which included infants with good iron status [6-8]. These findings increase the concern that early iron deficiency may lead to irreversible negative changes in long-term neurodevelopment, and accentuate the fact that maintaining adequate iron status is critical to the infant's neurological development. Since iron is a critical nutrient involved in brain development, it is recommended by Health Canada that babies' first complementary foods be iron-rich [9].

Although there is no current national data on iron deficiency in Canadian infants over the last 30 years, data from smaller studies suggests that iron deficiency anemia is a significant health problem [10]. For example, a study in Vancouver found that approximately 15% of breast-fed infants developed anemia at 8 months of age [11]. Further, the prevalence of iron deficiency anemia has been found to be even higher in preterm infants, and may be above 25% during their infancy [12].

The rationale in Canada of waiting 6 months before introducing solids to provide iron is not convincing. First of all, it is unclear whether data from current animal models sufficiently represents human iron metabolism. The iron content of mother's milk from species other than humans and cows is generally much higher [13]. Additionally, iron intakes of animals in the aforementioned studies were much higher than the daily iron intake of exclusively breast-fed infants per bodyweight. Secondly, since lactoferrin expressed in human milk is only 5% to 8% saturated with iron, it would be expected to have antibacterial properties [14]. Iron-binding proteins in human milk, including lactoferrin, may play an important part in resistance to infantile enteritis caused by *E. coli* [15,16]. This effect is abolished by saturating lactoferrin with iron. Therefore, the anti-pathogenic property of iron may be related to the binding forms of iron, rather than the amount of iron. Thirdly, early supplementation of iron may improve cognitive development of infants. In a double-blind, randomized study, Friel et al. demonstrated that healthy, breast-fed babies given iron supplementation between the ages of 1 and 6 months had better scores on the Bayley mental and psychomotor developmental indexes, as well as better visual acuity at 13 months of age than did the babies in the non-iron supplement group [17]. From this data, the American Academy of Pediatrics recommended that exclusively breast-fed full-term infants receive 1 mg/kg of iron supplementation per day, beginning at 4 months of age [18]. This policy supports the concept that the small amount of iron in human milk may not be enough for the physical and neurological development of exclusively breast-fed infants.

Why did the human species evolve to rely, during the first months of life, on an iron endowment instead of a continuous source of this element in mother's milk? In order to shed light on such an intriguing question, it must be analyzed from an evolutionary perspective. It is hypothesized that the environment in which babies were raised, as well as their exposures during the first months of life, were quite different in ancient times as compared to current conditions in developed countries. However, these ancient conditions were not necessarily worse than those of the less fortunate populations in the present day. In ancient times, continual exposure to pathogens from the environment and from food, capable of causing infectious diseases and threatening survival, constantly put the continuation of the human species at risk. This exposure was unavoidable and likely played a key role in shaping several mechanisms for infection prevention and host defense [19,20]. Among these mechanisms, those involving iron obtainment, metabolism, and utilization are of special interest, since iron is an essential element for survival and present in every cell in the body. Iron is also required for intracellular reactions involving certain commensal and pathogenic microbes which reside on the mucosal surfaces of the intestine [21]. Health Canada recommends that healthy, full-term infants should be breastfed until 6 months of age, at which point iron-rich complementary foods should be introduced. This recommendation is in accordance with the above hypothesis of auto-regulation in iron obtainment and utilization [9].

It is known that human milk is low in iron, and that the iron content in human milk is independent of maternal iron status in all cases except those involving severe maternal anemia [22-24]. This suggests regulation for transport of iron from the mammary glands into breast milk [19]. Interestingly, while iron in human milk declines during lactation [24], infants from 6 to 9 months develop an enhanced capacity to absorb iron, thereby avoiding iron deficiency [25]. Overall, such mechanisms might suggest that too much iron is not desirable. In fact, there has been speculation as to whether unrestrained absorption and excessive iron in the intestinal lumen might be detrimental. This harmful effect could lead to iron accumulation in tissues, which may lead to damage [26], or the creation of a supportive environment for pathogenic, iron-requiring bacteria [21]. Certainly, there are beneficial gut colonizing bacteria, such as lactobacilli and bifidobacteria, which do not rely on free iron. While lactobacilli are iron independent [27, 28], bifidobacteria harvest iron through scavenging compounds called siderophores [29] in order to thrive in the gut.

Thinking back to our ancestors, there are a few questions that become important. How did they cope with the low iron content in milk and the shrinking of the iron endowment between 4 and 6 months of life? Were they iron deficient? Were they anemic? One hypothesis is that the iron endowment used to be higher, owing to a greater transfer of maternal blood into the baby at birth. It is known that the modern day obstetric practice of early cord clamping after delivery reduces placental blood flow into the newborn, leading to an inferior iron status when compared to that of babies subject to delayed cord clamping [30,31]. As previously mentioned, another possibility is that environmental exposure was much higher, and occurred earlier in life as compared to the modern world. It is speculated that iron from soil, as well as the introduction of iron rich foods (maybe pre-chewed by mothers) [20] could have contributed to the prevention of iron deficiency conditions. Additionally, the ability to thrive in an environment in which exposure to pathogens was predominant may have led to the survival of the exposed individuals, allowing for their genes to spread.

From the studies discussed throughout this article, it is apparent that there is no clear answer to the proposed question. We know that our ancestors were able to thrive without any nutritional interventions, thereby suggesting that naturally acquired iron through mother's milk is satisfactory. On the other hand, it has been shown that iron deficiency, commonly seen in exclusively breastfed babies, can lead to negative physical and neurological deficits. The question therefore, remains unanswered. Future research should focus on identifying the pros and cons to either iron supplementation for infants, or lack thereof. It is vital to human health to gain more clarity on this topic, with the hopes of setting more evidence-based guidelines on iron requirements for future generations.

References

1. Lonnerdal B, Keen CL, Hurley LS (1981) Trace element metabolism in man and animals (TEMA)-4 (1stedn.) Griffen Press, Nestly, South Australia.
2. Domellof M, Lonnerdal B, Dewey KG, Cohen RJ, Hernell O (2004) Iron, zinc, and copper concentrations in breast milk are independent of maternal mineral status. Am J Clin Nutr 79: 111-115.
3. Fransson GB, Gebre-Medhin M, Hambraeus L (1984) The human milk contents of iron, copper, zinc, calcium and magnesium in a population with a habitually high intake of iron. Acta Paediatr Scand 73: 471-476.
4. Murray MJ, Murray AB, Murray NJ, Murray MB (1978) The effect of iron status of Nigerien mothers on that of their infants at birth and 6 months, and on the concentration of Fe in breast milk. Br J Nutr 39: 627-630.
5. Lozoff B, Georgieff MK (2006) Iron deficiency and brain development. Semin Pediatr Neurol 13: 158-165.
6. Lozoff B, Jimenez E, Wolf AW (1991) Long-term developmental outcome of infants with iron deficiency. N Eng J Med 325: 687-694.
7. Lozoff B, Jimenez E, Hagen J, Mollen E,Wolf AW (2000) Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. Pediatrics 105: E51.
8. Lozoff B, Jimenez E, Smith JB (2006) Double burden of iron deficiency in infancy and low socioeconomic status: a longitudinal analysis of cognitive test scores to age 19 years. Arch pediatr Adolesc Med 160: 1108-1113.
9. Health C, Canadian Paediatric S, Dietitians of C; Breastfeeding Committee for C (2012) Nutrition for healthy term infants: recommendations from birth to six months. Can J Diet Pract Res 73: 204.
10. Hartfield D (2010) Iron deficiency is a public health problem in Canadian infants and children. Paediatr Child Health 15: 347-350.
11. Innis SM, Nelson CM, Wadsworth LD, MacLaren IA, Lwanga D (1997) Incidence of iron-deficiency anaemia and depleted iron stores among nine-month-old infants in Vancouver, Canada. Can J Public Health 88:80-84.
12. Rao R, Georgieff MK (2009) Iron therapy for preterm infants. Clin Perinatol 36: 27-42.
13. Lonnerdal B (1990) Iron in human milk and cow's milk-effects of binding ligands on bioavailability. In: Iron metabolism in infants, CRC Press, Boca Raton.
14. Conneely OM (2001) Anti-inflammatory activities of lactoferrin. J Am Coll Nutr 20: 389S-395S.
15. Bullen JJ, Rogers HJ, Leigh L (1972) Iron-binding proteins in milk and resistance to Escherichia coli infection in infants. Br Med J 1: 69-75.
16. (1972) Lactoferrin--a bacteriostatic protein in human milk. Nutr Rev 30: 225-226.
17. Friel JK, Aziz K, Andrews WL., Harding SV, Courage ML, et al. (2003) A double-masked, randomized control trial of iron supplementation in early infancy in healthy term breast-fed infants. J Pediatr143: 582-586.
18. Baker RD, Greer FR; Committee on Nutrition American Academy of Pediatrics (2010) Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). Pediatrics 126: 1040-1050.
19. Quinn EA (2014) Too much of a good thing: evolutionary perspectives on infant formula fortification in the United States and its effects on infant health. American journal of human biology: the official journal of the Human Biology Council 26: 10-17.
20. Fomon SJ (2004) Assessment of growth of formula-fed infants: evolutionary considerations. Pediatrics 113: 389-393.
21. Markel TA, Crisostomo PR, Wang M, Herring CM, Meldrum KK, et al. (2007) The struggle for iron: gastrointestinal microbes modulate the host immune response during infection. J Leukoc Biol 81: 393-400.
22. Mello-Neto J, Rondo PH, Morgano MA, Oshiiwa M, Santos ML, et al. (2010) Iron concentrations in breast milk and selected maternal factors of human milk bank donors. J Hum Lact 26: 175-179.
23. Domellof M, Hemell O, Dewey KG, Cohen RJ, Lonnerdal B (2004) Factors influencing concentrations of iron, zinc, and copper in human milk. Adv Exp Med Biol 554: 355-358.
24. Shashiraj, Faridi MM, Singh O, Rusia U (2006) Mother's iron status, breastmilk iron and lactoferrin--are they related ?. Eur Jour Clin Nutr 60: 903-908.
25. Domellof M, Lonnerdal B, Abrams SA, Hernell O (2002) Iron absorption in breast-fed infants: effects of age, iron status, iron supplements, and complementary foods. Am J Clin Nutr 76: 198-204.
26. Lozoff B, Castillo M, Clark KM, Smith JB (2012) Iron-fortified vs low-iron infant formula: developmental outcome at 10 years. Arch Pediatr Adolesce Med 166: 208-215.
27. Weinberg ED (1997) The Lactobacillus anomaly: total iron abstinence. Perspect Biol Med 40: 578-583.

28. Wang B, Brand-Miller J, McVeagh P, Petocz P (2001) Concentration and distribution of sialic acid in human milk and infant formulas. Am J Clin Nutr 74: 510-515.
29. Vazquez-Gutierrez P, Lacroix C, Jaeggi T, Zeder C, Zimmerman M, et al. (2015) Bifidobacteria strains isolated from stools of iron deficient infants can efficiently sequester iron. BMC microbiology 15: 3.
30. Andersson O, Hellstrom-Westas L, Andersson D, Domellof M (2011) Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: a randomised controlled trial. BMJ 343: d7157.
31. Hutton EK, Hassan ES (2007) Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. JAMA 297: 1241-1252.