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Are Breastfed Infants Iron Deficient? The Question That Won't Go Away

Though iron is one of the most abundant elements in the earth's environment, iron deficiency is the most common single nutrient deficiency in the world. Given the very low iron content of human milk, there continues to be concern and controversy about the iron needs of the breastfed infant, particularly after 4-6 months of age when human milk alone will not supply the infant's requirement for iron.[1,2] In this volume of *The Journal*, Abrams et al[3] report on the potential iron deficiency in US breastfed infants 6-12 months of age, utilizing the database of dietary intakes from the 2016 Feeding Infants and Toddler Study (FITS).[4] This is a timely report as for the first time the Dietary Guidelines for Americans will include recommendations for the first 2 years of life when they are released in 2021. The guidelines for the intake of iron in breastfed infants will be controversial, no matter what is recommended. Compared with most other nutrients, iron has a narrow therapeutic window and historically there have been significant concerns for both too much and too little. The potential for both short- and long-term adverse neurodevelopmental outcomes of iron deficiency in infants continues to be an unresolved issue. This has lead the American Academy of Pediatrics to recommend universal iron supplementation for breastfed infants beginning at 4 months of age and continuing until appropriate iron-containing foods (including red meat and iron fortified cereals) are introduced into the diet.[1] These recommendations aim to minimize risks for iron deficiency with or without iron deficiency anemia, while waiting for unequivocal evidence that the very low iron content of human milk does not have an adverse impact on neurodevelopmental outcomes. The findings in this report give some support for this recommendation.

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It is significant that the recently published Scientific Report of the 2020 Dietary Guidelines Advisory Committee (to advise the Dietary Guidelines for Americans) concludes that "there is strong evidence that consuming complementary foods and beverages that contain substantial amounts of iron, such as meats or iron fortified cereals, helps maintain adequate iron status or prevents iron deficiency during the first year of life among infants with insufficient iron stores, or breastfed infants who are not receiving adequate iron from other sources." In this report, 2 nutrients, iron and vitamin D, are singled out for a discussion of dietary supplementation including food fortification, during the birth to 24 months life stage. However, the impact of iron supplements on neurodevelopmental outcomes in breastfed infants is not addressed.[2]

In the current report, the investigators examined the dietary intake data from infants 6-12 months of age who are either breastfed fed without infant formula (n = 296) or were mixed feeding (receiving both breast milk and infant formula) (n = 102).[3] It's notable that nearly all of the infants in both groups were also receiving complementary foods at the time of the FITS surveys. Though these investigators also looked at the formula-fed infants in the FITS survey, they concluded, as did the American Academy of Pediatrics[1] and the Dietary Guidelines Advisory Committee,[2] that infants fed formula (iron content 10-12 mg/L) but no breast milk, are at much less risk for significant iron deficiency and iron deficiency anemia. At present, approximately 75% of infants in the US are receiving some formula by 6 months of age, 43% receive formula without any breast milk, 32% receive both human milk and infant formula (mixed feeding); 25% are receiving no infant formula.[5]

Using the FITS data, Abrams et al calculated the iron intakes from 24-hour dietary recalls obtained by infant care providers. They then relied on the factorial modeling methodology utilized by the National Academy of Medicine (NAM) that determined the daily amount of iron needed to supply the estimated average requirement (EAR) in this age group is 6.9 mg per day.[6] This method takes into

EAR Estimated average requirement
FITS Feeding Infants and Toddler Study
NAM National Academy of Medicine

F.G. is co-author of the American Academy of Pediatrics position statement on iron deficiency and iron deficiency anemia in infants and toddlers.

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account the daily iron needed for increases in tissue (growth), iron stores, hemoglobin mass, as well as basal iron losses, mostly in feces. The EAR, the amount of nutrient intake that meets the needs of 50% of the population, is conventionally used to assess the nutrient status of a population, and is used in this study. The needs for an individual are assessed using the Dietary Reference Intake, which for iron in 6- to 12-month-old infants is 11 mg per day.[7] The Abrams study took this 1 step further and calculated the amount of daily iron absorbed in these infants, using absorption factors (also from the NAM) of 50% for breast milk iron, 20% for heme iron, and 5% for nonheme iron sources (eg, iron fortified cereals).[7] The absorbed iron requirement is 0.69 mg/day (10% of the EAR for intake) and is considered by the NAM as the daily physiologic requirement for iron. They then determined the percent of infants whose iron intakes were below the EAR. They also calculated the percent of infants whose absorption rates were below the physiologic requirement.

The results of their calculations are striking. Median iron intake in breastfed infants 6-12 months of age was only 3.3 mg per day, with 81.5 % of the infants having an intake of less than the EAR of 6.9 mg per day. Median iron intake of mixed fed infants was 9.6 mg per day, with 24.6% having an intake of less than the EAR (Table II in their report.) The median calculated amount of iron absorbed was 0.3 mg per day for breastfed infants and 0.5 mg per day for mixed fed infants, with 96% and 72% respectively, absorbing less than 0.69 mg per day needed to achieve the physiological requirement (Table III in their report). The sources of the absorbed iron are also revealing in the 2 groups. In the mixed-fed infants, 10% of absorbed iron was from human milk, 35% was from infant formula, and 44% was from grains (iron-fortified cereal). Nine percent was split evenly between vegetables, fruit, and meat. In breastfed infants (almost all of whom were receiving complementary foods), 25% of absorbed iron was from human milk, 52% from grains, 10% from meat, 7.5% from mixed dinners, and 5% from vegetables. Thus, the largest source of absorbed iron in both groups was from grains (iron-fortified cereals). Very little red meat was consumed by either group, despite current recommendations to the contrary.[1,2] It is disturbing that the authors note that the percentage of infants receiving iron-fortified cereals has decreased significantly since the previous FITS report in 2008, from 65% to 52% of infants.[3,4]

In the US, we have no current data on the prevalence of iron deficiency with or without anemia in infants between 4 and 12 months age. It is clear that the greatest calculated risk for iron deficiency as demonstrated in this report are those infants who are breastfed without additional sources of iron during this early stage of life. However, the degree and importance of iron deficiency in this population cannot be resolved without further additional clinical studies. First and most importantly, there must be an evaluation of the iron status of breastfed infants between the ages of 4 and 12 months with suitable biomarkers that are able to differentiate between iron deficiency and iron deficiency anemia. A hemoglobin determination alone will not provide this information. Three measures that provide discriminatory information for iron status include serum ferritin, reticulocyte Hb concentration, and serum transferrin receptor 1.[1] Second, it is noted that that iron absorption and metabolism is among the most complicated and most tightly regulated of any human nutrient. Studies of the control of iron regulation in this age group are desperately needed and must include the effects of iron supplements on this process, including its efficacy. Without this information, we will continue to ask the question for which there is no answer: Are breastfed infants iron deficient? ■

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