

See corresponding perspective on page 1261 and editorial on page 1277.

## Perspective: Putting the youngest among us into the nutrition “call for action” for food fortification strategies

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### ABSTRACT

Adequate iron intake is essential for optimal child development, but iron deficiency and anemia among infants and young children are widespread in low- and middle-income countries. Large-scale food fortification strategies hold great promise for reducing micronutrient deficiencies; however, for children <2 y of age, the impact of such strategies is limited because their intake of staple foods is relatively low and fortification levels are targeted at the adult population. Iron supplementation, iron fortification of foods targeted to infants, and point-of-use fortification with iron-containing products such as multiple micronutrient powders (MNPs) and small-quantity lipid-based nutrient supplements are evidence-based approaches recommended to reduce anemia among infants and young children when used in the right context. Since 2003, the WHO, with support from UNICEF, has recommended the use of MNPs to control iron deficiency. However, the percentage of children with anemia has changed very little over the past 10 y. Five years ago the UN declared a decade of action on nutrition, including World Health Assembly (WHA) targets for maternal, infant, and young child nutrition, yet the WHA set no anemia targets for children. In July 2020 the leaders of 4 UN agencies issued a call for action to protect children’s right to nutrition in the face of the COVID-19 pandemic and beyond. Given persistently high rates of anemia among young children, the negative developmental impact, the challenge of meeting iron needs from typical complementary food diets, and the availability of successful evidence-based fortification strategies for this age group, we encourage planners, speakers, and donors at this year’s UN Food Systems Summit and the Tokyo Nutrition for Growth Summit to 1) call for the WHA to set anemia targets for infants and young children and 2) promote investment in evidence-based interventions to improve the iron status of young children. *Am J Clin Nutr* 2021;114:1257–1260.

**Keywords:** infants and young children, nutrition, food fortification, micronutrient powders, complementary feeding, iron, malnutrition, anemia, LMICs

### Introduction

Large-scale food fortification strategies hold great promise for reducing micronutrient deficiencies in low-income populations (1). For infants and young children, however, the impact of such strategies may be limited because their intake of staple foods is relatively low and levels of fortification are targeted at the adult population (2). In particular, meeting iron needs from such sources is difficult for infants and young children <2 y of age, given their high iron needs to support blood volume

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Abbreviations used: LMIC, low- and middle-income country; MNP, multiple micronutrient powder; SQ-LNS, small-quantity lipid-based nutrient supplement; WHA, World Health Assembly.

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expansion, brain development, and tissue growth. Adequate iron intake is a prerequisite for optimal child development, yet iron deficiency remains persistently widespread in low- and middle-income countries (LMICs) (3, 4). About 60% of children <5 y of age in LMICs are anemic and rates are even higher at 6–24 mo (5, 6). Although the etiology of anemia is multifactorial, it is estimated that about half of cases are caused by iron deficiency (7). Given that the percentage of children with anemia has changed very little over the past 10 y, more work is needed to solve this persistent problem.

Five years ago the UN declared a decade of action on nutrition, including World Health Assembly (WHA) targets for maternal, infant, and young child nutrition, yet the WHA set no anemia targets for children. In December 2020, the Nutrition for Growth Year of Action was initiated (8). This year will culminate in the UN Food Systems Summit in September 2021 and the Tokyo Nutrition for Growth Summit in Japan in late 2021 (9, 10). We fully support this international effort to combat malnutrition; however, with respect to iron deficiency, the most vulnerable age group (6–24 mo) has been largely left out of the “call for action,” which has emphasized large-scale food fortification or biofortification for the general public.

### Challenges in achieving adequate iron intake by infants and young children

Iron stores at birth are generally sufficient to meet the needs of exclusively breastfed infants for  $\geq 6$  mo, assuming delayed umbilical cord clamping (11). After 6 mo, iron from non-breast-milk sources is needed. At 6–12 mo of age, estimated average iron requirements are 6.9–8.0 mg/d and the recommended dietary intake is 11 mg/d, assuming absorption of 10% (12, 13). At 1–3 y, iron needs are lower than at 6–12 mo: the estimated average iron requirement is 3–5 mg/d and the recommended dietary intake is 7 mg/d (12, 13). Although iron needs in these age intervals are well understood, estimates of iron absorption from different foods and under various conditions (such as iron deficiency) vary widely. Absorption from plant-based foods, particularly those with high concentrations of phytate, is likely to be <10%.

For breastfed infants not receiving fortified products, achieving adequate iron intake after 6 mo of age is challenging (14). Human milk contains relatively little iron ( $\sim 0.35$  mg/L) (12). Absorption of iron from human milk is variable (11), but even if 100% is absorbed, iron intake from 600 mL human milk would be only  $\sim 0.2$  mg/d. As a result, nearly 100% of the recommended intake of 11 mg/d needs to come from sources other than human milk, i.e., complementary foods. Because breastfed infants have high iron needs but consume small amounts of complementary foods ( $\sim 200$ – $300$  kcal/d) (15), the iron density of those foods (mg Fe/100 kcal) needs to be very high—9 times higher than required for adult men (14).

In many populations, iron intake from typical complementary foods is far below the amount needed. Even with “best case scenario family food menus,” the iron density of the hypothetical infant diet among low-income households in Guatemala or India would be far below the target (16, 17). Linear programming analyses have demonstrated that iron requirements for infants could be met without fortified foods, but only if liver were consumed daily (18). With more realistic (but not necessarily affordable)

diverse dietary patterns that include grains, legumes, egg, green leafy vegetables, and fish or chicken, only 26%–37% of iron needs at 6–8 mo and 35%–52% of iron needs at 9–12 mo could be met. In the second year of life, inadequate iron intake is still prevalent (16, 19), but with careful selection of foods it is somewhat easier to meet iron needs than is the case at 6–12 mo (20).

Large-scale food fortification of staple foods is unlikely to fill the gap in iron intake of infants. For maize or wheat flour, the amount of fortification recommended is 60 mg/kg flour (using ferrous sulfate or ferrous fumarate) (21). If 50% of the energy needed from complementary foods is provided by fortified maize or wheat flour, infants could consume 100 kcal/d ( $\sim 27$  g/d) of flour at 6–9 mo and 150 kcal/d ( $\sim 40$  g/d) at 9–12 mo, which would provide 1.6 and 2.4 mg Fe/d (14% and 22% of the RDA), respectively. After 12 mo, consumption of 275 kcal/d of fortified maize or wheat flour would provide 4.5 mg Fe/d, which is 64% of the RDA, a much more substantial contribution than is possible during infancy.

Similarly, biofortification of staple foods is likely to fall short of meeting the iron needs of infants. At the highest concentration of iron achieved in biofortified pearl millet and beans ( $\sim 86$  mg/kg) (22), the amount of iron provided by 100 and 150 kcal/d of those foods would be 2.4 and 3.6 mg/d (22% and 32% of the RDA), respectively. After 12 mo, the amount of iron provided by 275 kcal/d of those foods would be 6.6 mg/d (94% of the RDA). These estimates for large-scale food fortification and biofortification all assume 10% iron absorption, which may be a reasonable assumption for young children with iron deficiency (23) but is likely an overestimate for a healthy population. In addition, it may be unrealistic to assume that infants or toddlers could consume the required amounts (100–275 g) of cooked beans or millet per day, every day. Thus, for *prevention* of iron deficiency, these approaches are insufficient for infants, although they hold promise for toddlers >12 mo of age, assuming the required quantities can be consumed.

### Evidence-based solutions available

Iron supplementation, targeted food fortification with iron, and point-of-use fortification with iron-containing products such as multiple micronutrient powders (MNPs) and small-quantity lipid-based nutrient supplements (SQ-LNSs) are evidence-based approaches recommended to address the anemia burden in infants and young children when used in the right context (24–28). These interventions are generally efficacious in increasing ferritin and hemoglobin concentrations and reducing anemia prevalence; however, it should be noted that there are important non-nutrient-related causes of anemia including malaria, chronic inflammation, and recurrent infections, all of which need to be addressed in comprehensive programs to control anemia. Moreover, systemic inflammation can reduce iron absorption and serum iron concentration and is related to increased serum ferritin concentration, a measure of iron stores but also an acute phase reactant. Thus, biochemical surveillance of effectiveness is challenging and, if inflammation is prevalent, there is a risk of underestimating iron deficiency when it is assessed using serum ferritin.

Iron supplements (drops or syrup) have been successfully used for the treatment of iron deficiency anemia, but their effectiveness in noncontrolled environments is markedly affected

by minor adverse consequences, including strong metallic taste and teeth staining (29, 30). Recognizing a lack of impact of iron supplementation on anemia prevalence in national and subnational programs, there is a growing focus on alternative ways to provide iron.

Targeted food fortification, i.e., foods specifically formulated for infants and young children, can allow for a level of fortification much higher than is possible for the general public. Fortified blended foods, such as corn–soy blend, are examples of targeted foods that are efficacious for improving iron status (26, 27).

Since 2003, the WHO, with support from UNICEF, has recommended the use of “home” or “point-of-use fortification” with MNPs to control iron deficiency, stating that: “In populations where the prevalence of anaemia in children under 2 years of age or under 5 years of age is 20% or higher, point-of-use fortification of complementary foods with iron-containing micronutrient powders in infants and young children aged 6–23 mo is recommended, to improve iron status and reduce anaemia” (31). According to the most recent Cochrane review, MNP supplementation is associated with an 18% reduction in anemia and a 53% reduction in iron deficiency (24). In 2018, 18 million children in 54 countries were reached with MNPs, but this only represents ~5% of those with anemia (32). Because of issues related to a lack of local champions, a change in the financing model, and the COVID-19 pandemic, fewer countries are currently (2021) distributing MNPs to fewer children. The inevitable results will be higher rates of iron deficiency and anemia.

The evidence base regarding efficacy of SQ-LNSs has grown substantially in the past 10 y. Recent systematic reviews have demonstrated a 16%–21% reduction in anemia (25, 33), a 56% reduction in iron deficiency (33), and a 64% reduction in iron deficiency anemia (33) when SQ-LNSs are provided, similar to the efficacy of MNPs. SQ-LNSs also reduce the risk of impaired growth (34) and development (35), as well as mortality (36). Neither MNPs nor SQ-LNSs were developed to replace a varied age-appropriate diet for young children, but each plays a role in improving diets that may be inadequate in some essential nutrients.

Provision of iron in any product aimed at infants and young children raises questions of safety with regard to potentially increased risk of certain infections such as malaria and diarrhea (37), although a recent Cochrane review concluded that MNPs did not increase diarrhea, upper respiratory infection, malaria, or all-cause morbidity (24). This potential risk may be related to the dose of iron: further research is needed on how to optimize the amount (and form) of iron provided so as to prevent iron deficiency and anemia while minimizing the risk of adverse outcomes. Although the net health benefits of fortified products such as MNPs may be context specific, for most countries they appear to be positive (38).

### Need for advocacy and implementation research

With rates of iron deficiency and anemia in infants and young children as high as 60%–70% in South Asia and only slightly lower in Sub-Saharan Africa, and evidence-based interventions available to control iron deficiency, it appears that the global nutrition community has failed to prioritize this critical health issue.

In July 2020 the leaders of 4 UN agencies (UNICEF, the FAO, the World Food Programme, and the WHO) issued a call

for action to protect children’s right to nutrition in the face of the COVID-19 pandemic (39). They called for promoting access and investing in improved maternal and child nutrition through pregnancy, infancy, and early childhood. They advocated for a swift response and investments from governments, donors, the private sector, and the UN. This year’s UN Food Systems Summit and the Tokyo Nutrition for Growth Summit were designed to support and enhance this call for action.

The WHA set a target of a 50% reduction of anemia in women of reproductive age by 2025 (40). Given the stubbornly high rates of anemia among young children, the negative developmental impact, the challenge of meeting iron needs from typical grain-based complementary diets, and the availability of successful evidence-based fortification strategies for this age group, we encourage planners, speakers, and donors at this year’s UN Food Systems Summit and the Tokyo Nutrition for Growth Summit to 1) call for the WHA to set similar anemia targets for infants and young children and 2) promote investment in evidence-based interventions to improve the iron status of young children.

Anemia among young children persists as a global health problem for many reasons including a lack of political awareness, programmatic limitations regarding delivery of iron interventions, reduced efficacy in the presence of infection or inflammation, and nonnutritional causes of anemia. Given the lack of progress over the past decade, greater research is needed on the sustainability of evidence-based interventions and the factors that enhance or impede implementation. To date, home fortification programs have been paid for and implemented through UN agencies and the public sector in individual countries, but these sources of financing are not guaranteed over the long-term. There is an urgent need to find alternate sources of funding for such programs, such as blended finance solutions to pay for the products.

Given the critical role of nutrition in supporting child development and subsequent human capital formation, we must heed the combined UN call for action to protect children’s right to nutrition, not just during the COVID-19 pandemic but with solutions that are sustainable for the future. These should include the prevention of iron deficiency with evidence-based interventions targeted at children <2 y old.

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