

Food-Based Complementary Feeding Strategies for Breast-Fed Infants

What's the Evidence That It Matters?

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The period of complementary feeding represents a major portion of the 1000-day critical window and thus impacts a period of substantial and dynamic infant development. This review highlights and synthesizes findings of several recent studies conducted to evaluate food-based strategies on outcomes related to micronutrient status, growth, and neurocognitive development. Particular emphasis is placed on interventions using meat or fortified products to impact iron and zinc intakes, because of the dependence of breast-fed infants on complementary food choices to meet requirements for these 2 critical micronutrients. Regular consumption of modest amounts of meat or fortified cereals provides adequate absorbed zinc to meet estimated physiologic requirements, whereas homeostatic adaptation to lower zinc intake from unfortified cereal/plant staples is inadequate to meet requirements. Iron fortification of cereals may be somewhat more effective than meat to improve iron status, but neither prevents iron deficiency in breast-fed infants, even in westernized settings. Improvements in the quality of complementary foods have had very modest effects on linear growth in settings where stunting is prevalent. Maternal education is strongly associated with both linear growth and with child neurodevelopment. The determinants of early growth faltering are more complex and intractable than "simple" dietary deficiencies. Solutions to growth faltering in young children most likely need to be multidimensional and almost certainly will need to start earlier than the complementary feeding period. *Nutr Today*. 2014;49(6):271–277

Improving the quality of complementary feeding has been cited as second only to improved rates of exclusive breast-feeding as a measure to prevent deaths in young children in low-resource settings.^{1,2} Indeed, the period of complementary feeding covers at least half of

the "1000-days" critical window, the period from conception to a child's second birthday.³ This period of rapid development has been identified as a crucial time to improve children's health and well-being. Since in reality, the minority of infants are exclusively breast-fed for the first 6 months of life,^{4,5} the period of complementary feeding actually includes a much larger portion of the window and thus impacts a period of substantial and dynamic infant development (Figure).

The term "complementary foods" has been defined in many ways but generally refers to any nutrient- and energy-containing solid or semisolid food or liquid consumed by infants in addition to human milk or formula. The term "weaning foods" is also applied to indicate that this is a transition from the full liquid diet of the young infant to a more diverse diet, which eventually merges to become the same as the rest of the family's foods. For the purposes of this brief review, the emphasis is on breast-fed infants, for whom complementary foods ideally balance or "complement" the nutritional gaps that develop as a result of the dynamic nutritional composition of human milk and of the nutritional needs of the breast-fed infant. Although the variety of food choices for older infants and toddlers range widely in industrialized settings compared with lower-resource settings, practices in all settings seem to be strongly influenced by traditions, often more so than biological factors.

The relative nutritional importance of the choice of types of foods differs according to the type of infant feeding that has been undertaken, that is, whether an infant has been exclusively (and adequately) breast-fed or has received a standard infant formula. The latter provides generous amounts of all essential micronutrients and thus leaves little risk of micronutrient deficiencies, although there are tradeoffs for that benefit. Formula-fed infants may be at more risk of overfeeding, and discussions regarding complementary feeding for this large group have focused more on choices to minimize excessive weight gain. Of course, in the real world, many infants do not fall neatly into one category or the other, especially in industrialized countries. In the United States, many infants receive a combination of human milk and formula; the balance of the intake coming from each source will largely define the risk of micronutrient deficiencies. Nevertheless, the rates of "breast-feeding

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1000 Days Critical Window

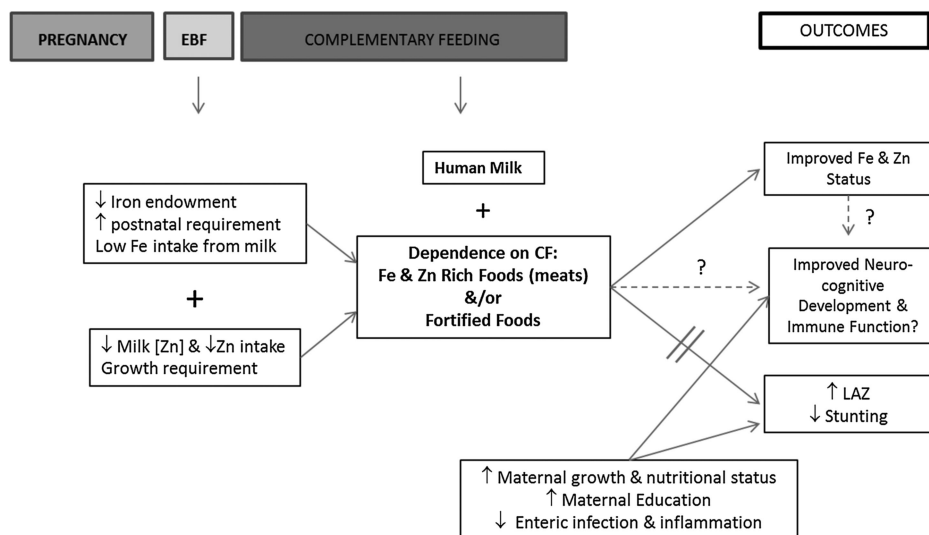


FIGURE. Conceptual diagram for postnatal phases of the 1000-day critical window on iron (Fe) and zinc (Zn) status, risk of deficiencies, and potential impact of complementary feeding on outcomes. Abbreviations: CF, complementary foods; EBF, exclusively breast fed; LAZ, length-for-age Z score.

only” (no formula) have been steadily increasing in the United States. The annual “Breastfeeding Report Card” from the Centers for Disease Control and Prevention indicates that nearly half of all infants (47%) in the United States are breastfed for 6 months, with 16.3% being exclusively breast-fed at 6 months, thus aligning with current recommendations to exclusively breast-feed through about 6 months.^{5,6} Furthermore, a full quarter of infants in the United States are still breast-fed at 12 months of age. These figures for breastfeeding in the United States emphasize the importance of complementary food choices. The risks of micronutrient deficiencies in breast-fed infants are not only relevant to low-resource settings, where breast-feeding is more likely to be the norm.

Because breast-feeding is recognized as the criterion standard for infant feeding, this review will focus on evidence for the impact of complementary feeding on outcomes related to nutritional status, growth, and development in breast-fed infants. The discussion is not intended to be a comprehensive review of the fairly extensive literature on complementary feeding, especially in international settings, but rather will highlight and synthesize findings of several recent studies conducted by our research group to evaluate food-based interventions on selected outcomes (Table).

NUTRITIONAL GAPS FACED BY OLDER BREAST-FED INFANTS

The risk of micronutrient deficiencies in breast-fed infants and the dependence on complementary foods has been reviewed extensively.^{7,8} Iron and zinc are 2 micronutrients particularly recognized as “problem nutrients”

for older breast-fed infants.⁹ This is due to a combination of factors. Human milk is very low in iron, and even with its favorable absorption, the amount is too modest to contribute substantially to nutritional requirements. For the first several months of life, the infant relies on the iron “endowment” at birth, including the stores acquired in utero and that which is available from red blood cells after birth. Without fortification, plant-based diets are generally low in iron and/or contain compounds that interfere with its absorption. In low-resource settings, the high rates of infection and chronic immunostimulation are likely to stimulate the synthesis of hepcidin, a protein that blocks absorption of iron from the intestine, among other effects.¹⁰ The degree to which chronic “immune stimulation” in low-resource settings contributes to iron deficiency is unquantified, but is likely to be a factor contributing to the very high rates of iron deficiency in young children. By approximately 6 months of age, breast-fed infants become reliant on complementary foods to meet their iron requirements, which are relatively high because of the need to expand their red blood cell mass.

In the case of zinc, the underlying basis for risk of deficiency is different from that of iron. Zinc concentrations in human milk are initially very high and will provide a comfortable margin well above the estimated dietary requirement.¹¹ Because of complex interactions of zinc transporters in the mammary gland,¹² the concentration of zinc in human milk falls precipitously, regardless of maternal dietary zinc intake or status.¹³ By approximately 6 months, intakes from human milk will, like iron, provide only a fraction of estimated requirement. The breast-fed infant thus becomes dependent on choice of complementary foods to meet requirements for both of these 2 essential trace minerals.

TABLE Summary of Highlighted Complementary Feeding (CF) Interventions

Study	Setting	Subjects	Intervention	Outcomes	Results/Comments
Krebs et al ^{15,16}	Denver, Colorado	42; 5- to 9-mo-old breast-fed (only) infants	Randomized to first CF of M, IFZC, or IFC	M, IFZC, or IFC Dietary intake Zinc absorption (CF + human milk) Zinc and iron status at 9 mo of age	<ul style="list-style-type: none"> • Zinc intake and daily absorbed zinc for M and IFZC group significantly greater than IFC group • Zinc absorption for IFC only ~50% of physiologic requirements • Iron intake IFZC and IFC group significantly greater than M group • M group had more infants with elevated soluble transferrin receptor • Independent of group, ~1/3 of subjects were iron deficient, 36% anemic
Krebs et al ¹⁸	Guatemala, Democratic Republic of Congo, Zambia, Pakistan	20 clusters/arm; 1062 infants (n = 530 meat, n = 532 cereal); 6- to 18-mo-olds	Cluster randomized efficacy trial: daily meat vs multiple micronutrient-fortified cereal x 1 y	<ul style="list-style-type: none"> • Linear growth velocity • Micronutrient status • Neurocognitive development (Bayley Scales of Infant Development) 	<ul style="list-style-type: none"> • No difference by group in linear growth • From baseline (6 mo) to 18 mo, stunting rates increased from 33% to ~50% (not different by group) • Maternal education and maternal height positively associated with linear growth velocity • Anemia rates did not differ by group; iron deficiency was lower in cereal group • Mental and psychomotor scores not different between groups (behavior scale favored meat group)
Tang et al ²⁶	Yunnan Province, China	20 clusters, meat (n = 514); 40 clusters cereal (n = 957); 6- to 18-mo-olds	Cluster randomized trial: daily M vs C x 1 y	<ul style="list-style-type: none"> • Linear growth velocity • Neurocognitive development (Bayley Scales of Infant Development) 	<ul style="list-style-type: none"> • Linear growth of M group greater than C group • LAZ negative at 6 mo and continued to decline over course of study • Mental and psychomotor scores slightly but significantly favored meat group

Abbreviations: C, cereal; IFC, iron-fortified cereal; IFZC, iron- and zinc-fortified infant cereal; LAZ, length-for-age Z score; M, meat.

The foods that provide naturally good sources of both iron and zinc are meats/flesh foods and organs such as liver. Traditionally, however, in industrialized countries, these have been among the last foods to be introduced to infants. Instead, iron-fortified cereals (and infant formulas) have been the recommended “first food” for infants; these are followed by pureed vegetables and fruits, none of which provide significant amounts of either iron or zinc. Recommendations from the World Health Organization for complementary feeding practices emphasize the importance of daily animal source foods to meet micronutrient needs, including especially iron and zinc. If such foods are not consumed, routine use of supplements or fortified foods is recommended.¹⁴ Although the theoretical benefit of meat as a complementary food is sound, the actual data to demonstrate benefit have been very limited.

EVIDENCE FOR THE MICRONUTRIENT ADEQUACY OF DIFFERENT COMPLEMENTARY FEEDING STRATEGIES

Controlled trials comparing complementary feeding strategies to meet iron and zinc needs of older infants are limited. We applied stable isotope techniques to examine the adequacy of complementary foods available in the United States, which were either fortified (infant cereals) or contained intrinsic, highly bioavailable zinc and iron (meats).^{15,16} The extent to which an older breast-fed infant could adapt to chronic low intakes of zinc by increasing absorption efficiency was also of interest, so we also included a whole-grain infant cereal that was fortified with iron but not with zinc (Table 1).

In terms of zinc intake and absorption, the results of this study supported the premise that, in combination with ad libitum breast-feeding, either meat or a zinc-fortified cereal would approximate intake and absorption similar to the Estimated Average Requirement and physiologic requirements, respectively, of the Institute of Medicine.¹⁷ Reflecting the low concentrations in human milk after 6 months of lactation, the contribution of zinc from breast milk was less than 10% of the day's total intake, even though it was well absorbed. The infants receiving the cereal not fortified with zinc fared less well, with a daily intake that averaged approximately half the Estimated Average Requirement, including the zinc from human milk. Absorption efficiency did not adequately compensate for the low intake, and in this group, none of the infants' daily absorbed zinc reached the estimated physiologic requirement. The unfortified cereal group tended to have the lowest exchangeable zinc pool size, consistent with their significantly lower absorbed zinc.¹⁵

The findings for iron status were more heterogeneous among these 9- to 10-month old infants. Iron-fortified cereals have traditionally been considered an important means to meet the

relatively high iron requirements of the older infant. Although the iron in meat is in the heme form and is thus much more bioavailable than that of the electrolytic iron fortificant in the cereal, the total amount is less than that in typical fortified cereals. Evidence to support the adequacy of meats at feasible intakes as a source of iron was also very limited. As expected, the iron intakes for the infants assigned to the fortified cereals were several-fold higher than that of the infants receiving meats. There were no statistically significant differences among the groups in the mean ferritin levels, but more infants in the meat group had a high soluble transferrin receptor, suggesting more suboptimal iron status. Somewhat surprisingly, however, regardless of feeding group, more than a third of these healthy, well-nourished infants were mildly anemic and had evidence of iron deficiency. Dietary iron intake was not correlated with iron status; rate of weight gain between 5 and 9 months was negatively associated with serum ferritin level. These findings emphasize that such factors as the accessible endogenous iron at birth, rate of postnatal growth, and infant size, in addition to dietary intake and bioavailability, all contribute to infants' iron status.¹⁶

In a larger multicountry cluster randomized trial, we compared the efficacy of a year of daily consumption of 1 to 1.5 oz of meat versus a multiple micronutrient-fortified cereal product on nutritional outcomes, including iron and zinc status, in predominantly breast-fed infants and toddlers in low-resource settings. This trial was conducted in Guatemala, Democratic Republic of Congo, Pakistan, and Zambia, all sites where stunting rates in the second year of life were greater than 40%¹⁸ (Table). Similar to the study of US breast-fed infants described above, the iron intake of the fortified cereal group was ~3.5 times that of the meat group, and the iron status was more favorable in the cereal group. The rate of anemia, however, was modest in both groups at the end of the intervention period at 18 months, with 27% and 16% in the meat and cereal groups, respectively ($P = .001$). Although no control group without any intervention was available for comparison, these rates are lower than generally expected in such settings, suggesting that the iron status of both groups was improved. Zinc content of the cereal was essentially equivalent to that of the meat, and mean plasma zinc concentrations did not differ by group, although the means were quite low compared with the US infants, possibly reflecting subclinical inflammation.¹⁸

These studies illustrate several points. First, the absorption efficiency (fractional absorption) of zinc from human milk was relatively high, but the actual amount of zinc absorbed was still low and did not adequately compensate for the low intake. This confirms the dependence of the older infant on complementary food sources to get enough zinc. In addition, the zinc intake of the unfortified cereal group, which followed a pattern very common in both the United States

and especially in many developing countries (ad lib human milk, fruits and vegetables, and unfortified cereal), resulted in daily absorbed zinc well below the estimated requirement. “Up-regulation” of absorption of the zinc with this dietary pattern was insufficient to meet requirements, leaving this group at clear risk of mild zinc deficiency. In low-resource settings, the risk for deficiency is even higher because of greater reliance on unfortified cereal/plant staples and high incidence of diarrhea episodes, which often result in increased zinc losses and thus result in a relatively higher requirement. Second, the absorption from the fortified cereal was similar to that of the meat, confirming that zinc fortification of a relatively low-phytate food offers an efficacious means of meeting zinc requirements of older infants. Third, with respect to iron, although the meat groups had somewhat more evidence of deficiency, substantial numbers of the infants from all groups were iron deficient. The fact that dietary intakes at or above recommended levels did not ensure good iron status illustrates the complexity of iron nutrition in older infants and toddlers and likely provides further insight into the very high prevalence of deficiency in low-resource settings.

The metabolic data comparing food-based approaches to complementary feeding indicate that daily intakes of a modest amount of meat are feasible to meet recommended intakes of zinc. However, even with the more favorable bioavailability of heme iron, they may not be sufficient to maintain normal iron stores or, especially to achieve repletion in a state of deficiency. It is also clear, however, that iron status is complicated by factors other than dietary intake.

EVIDENCE FOR IMPACT OF IMPROVED COMPLEMENTARY FEEDING ON GROWTH

Growth faltering is very common, and improving the quality of complementary feeding is one of the strategies often cited to improve growth, specifically to reduce stunting (≤ -2 length-for-age Z [LAZ] score). The basis for this emphasis is several-fold. The most prevalent pattern of growth faltering is in linear growth, with overall stunting rates estimated to be approximately one-third of infants and children younger than 5 years in low-resource settings.¹⁹ In addition, mean LAZ scores at birth are often below the median and continue to steadily decline through the first 24 months of life, tending to plateau thereafter.²⁰ Because exclusive breast-feeding is recommended for the first 6 months of life, and many efforts have focused on improving this health behavior, the remaining postnatal window of opportunity is from 6 to 24 months, the period of complementary feeding. Wasting rates are generally much lower than stunting rates, and mean weight for length Z scores is near the median, which suggests

that energy intake and quantity of food are less problematic compared with the challenge of providing high-quality complementary foods.

With the recognition that energy intake is not generally growth limiting, the focus of attention has been on intake of micronutrients and quality of complementary foods, less so than quantity, although the importance of adequate energy intake cannot be ignored. As noted above, the World Health Organization recommends daily intake of meats and animal source foods for infants and toddlers as routine complementary foods, the rationale for which is supported by the metabolic studies described above. Evidence for efficacy of meats as complementary foods to impact growth faltering in low-resource settings has been limited primarily to observational and epidemiologic data,^{21–23} many supporting an association of better growth and development with regular consumption of meat. One education intervention in Peru specifically encouraged regular consumption of “special foods,” including daily eggs, fish, or chicken liver as a complementary food. Results of this cluster randomized trial included a significant reduction in stunting rates.²⁴ Lacking, however, had been controlled efficacy trials specifically testing the impact of daily meat consumption on linear growth. We have undertaken 2 cluster randomized trials in diverse settings with high rates of stunting in which 6-month-old infants were provided daily meat for 1 year; their growth rates were compared with infants who received micronutrient-fortified cereal²⁵ (Table 1). Although in both studies both meat and fortified cereal groups likely experienced improvements in their micronutrient status from the interventions, no or modest effects on linear growth velocity and stunting were observed.^{18,26}

Notably, in these meat intervention studies, as well as in many other trials testing other interventions to improve complementary feeding,²⁷ the impact on linear growth has been quite modest. Even when statistically significant increases have been achieved,²⁶ the effect size or absolute difference in centimeters has been small.²⁸ Furthermore, none of the interventions have stopped the downward trajectory in LAZ from infancy into the second year of life that is common in austere settings.²⁰ Similarly, interventions in older infants and toddlers to specifically improve micronutrient intakes by home fortification with multiple micronutrient powders have not impacted growth.²⁹ It is possible that, in settings with early and severe stunting, the nutritional deficits may require higher-than-normal nutrient intake to provide essentially a therapeutic effect. Simply improving the basic quality of complementary feeding through single foods (eg, meats) or micronutrient-fortified foods thus may not provide a potent enough growth “signal.” Our interpretation of these observations is that the determinants of stunting are considerably more complex than nutritional intake (including of micronutrients), and nutritional status during the postnatal period. Evidence of

this is supported by our observations and experience in Guatemala, where stunting is highly prevalent in infants and toddlers and persists into adulthood. Mean LAZ was already -2 by 6 months, and nutritional interventions initiated at 6 months have had no impact on progressive linear growth failure at 12 and 18 months of age.^{18,30} Maternal height is strongly correlated with infant length and rate of linear growth.^{18,31} Chronic inflammation, for example, as associated with environmental enteropathy and intestinal inflammation, has also been suggested to adversely impact linear growth in this age group.^{32,33} Finally, in the multicountry meat versus fortified cereal study, the strongest predictor of linear growth was maternal education.¹⁸

EVIDENCE FOR IMPACT OF IMPROVED COMPLEMENTARY FEEDING ON NEUROCOGNITIVE DEVELOPMENT

Compared with investigations of growth and nutritional status, fewer interventions have investigated the impact on neurocognitive development of improving the quality of complementary feeding. Undoubtedly, developmental deficits do not occur in isolation and are strongly correlated with stunting and poverty.³⁴ In the trials described briefly above, we have observed modestly but significantly greater scores on behavioral subscales (unpublished observation), but no meaningful differences in mental or motor development.^{18,26} One recent study using lipid-based nutrient supplements or a micronutrient-fortified corn-soy flour found no difference in developmental scores in 18-month-old Malawians after a yearlong intervention, but LAZ gain and maternal education were both significant predictors of developmental outcomes.³⁵ In a trial in Indian toddlers, improved complementary feeding alone did not affect development, but complementary feeding guidance along with psychosocial stimulation had a significant effect on the toddlers' mental development compared with children in the control group.³⁶ These findings all support the critical importance of maternal education, and there is likely a synergistic effect of higher maternal education, enhanced child psychosocial stimulation, and improved nutritional status on child development, with or without a substantial impact on linear growth.

SUMMARY

The period of complementary feeding encompasses more than half of the "1000-day window of opportunity." Older breast-fed infants are clearly at outstanding risk for iron and zinc deficiencies if complementary food choices do not include rich sources of these micronutrients. This is due to the biology of human milk and the dynamic changes in nutritional requirements during later infancy and toddlerhood. Although this risk applies to breast-fed infants in industrialized countries, it is likely to be even greater in

low-resource settings, where recurrent infections likely contribute to altered nutrient bioavailability, as for iron due to hepcidin stimulation, and to increased losses, as for zinc due to recurrent diarrhea. Improvements in complementary feeding, both with use of fortified foods or by regular consumption of meats, have been associated with improvements in the nutritional status for both iron and zinc. In 3 intervention studies, we have demonstrated good acceptance of meat by 6-month-old infants, and in many settings, flesh foods and/or organ tissue may be more readily available than fortified food products.^{23,25,36} These beneficial effects warrant continued targeting of complementary foods to supply these 2 critical micronutrients. While improved intakes and status have been achieved, the impact of complementary feeding interventions on stunting, however, has been very modest, suggesting that the determinants of growth faltering are more complex and intractable than "simple" dietary deficiencies. Solutions to growth faltering in breast-fed infants and young children likely need to be multi-dimensional and almost certainly will need to start earlier.

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