

Complementary feeding: clinically relevant factors affecting timing and composition¹⁻⁴

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ABSTRACT

Exclusive breastfeeding for the first 6 mo of life followed by optimal complementary feeding are critical public health measures for reducing and preventing morbidity and mortality in young children. Clinical factors, such as birth weight, prematurity, and illness, that affect the iron and zinc requirements of younger infants are discussed. Maternal diet and nutritional status do not have a strong effect on the mineral content of human milk, but physiologic changes in milk and the infants' status determine the dependence of the infant on complementary foods in addition to human milk to meet iron and zinc requirements after 6 mo. The nature of zinc absorption, which is suitably characterized by saturation response modeling, dictates that plant-based diets, which are low in zinc, are associated with low absolute daily absorbed zinc, which is inadequate to meet requirements. Foods with a higher zinc content, such as meats, are much more likely to be sufficient to meet dietary requirements. Current plant-based complementary feeding patterns for older fully breastfed infants in both developed and developing countries pose a risk of zinc deficiency. The strong rationale for the potential benefits of providing meat as an early complementary food, and the examples of successful intervention programs, provide potent incentives to pursue broader implementation programs, with concurrent rigorous evaluation of both efficacy and effectiveness. *Am J Clin Nutr* 2007;85(suppl):639S-45S.

KEY WORDS Zinc, iron, meat, zinc absorption, breastfeeding, breastfed infant

INTRODUCTION

Improving the quality of complementary foods has been cited as one of the most cost-effective strategies for improving health and reducing morbidity and mortality in young children. Recent estimates are that nearly one-third of child deaths could be prevented by a combination of exclusive breastfeeding for 6 mo, optimal complementary feeding practices, and zinc and vitamin A supplementation (1-3). The importance of the period of complementary feeding is further emphasized by recognition not only that $\approx 50\%$ of all childhood mortality is directly or indirectly related to malnutrition, but also that the first 2 y of life represents a critical window of vulnerability. In many regions, the onset of stunting is within the first few months of life (4), and wasting and undernutrition progressively continue through the first 2 y of life (4, 5). Economic analyses suggest that the challenge of achieving optimal feeding for infants and toddlers is often as much related to ignorance about feeding and food choices as to scarcity of food.

In the United States, as with global efforts, promotion of increased breastfeeding rates and duration has appropriately been a major emphasis of public health policy. Less emphasis has been given specifically to complementary feeding and nutrition issues particular to older breastfed infants. This article summarizes some of the infant and maternal factors that influence the ideal timing and composition of complementary feeding to meet the nutritional requirements of breastfed infants. Emphasis will be given to the 2 trace minerals iron and zinc, deficiencies of which are particularly common in older infants and toddlers.

CLINICAL FACTORS AND NUTRIENT REQUIREMENTS

Term infants are normally born with stores or metabolically active pools of many nutrients. This is in contrast with preterm infants, who miss a substantial portion of the beneficial and rapid third-trimester accretion of nutrients. This poses a particular challenge to breastfed preterm infants if human milk fortifiers are not readily available. In developing countries, particularly in certain regions such as south Asia, very high rates of low birth weight are associated with increased vulnerability to undernutrition and to infectious morbidity, which may further increase nutrient requirements. Distinctions between small-for-gestational-age (SGA) term infants and low birth weight due to modest prematurity are often not clear in data from developing countries, and nutritional vulnerability may differ in these 2 circumstances.

Two examples illustrate altered in utero transport or accretion of micronutrients. Infants of diabetic mothers have been shown to have reduced brain iron concentrations and iron stores, which are reflected by lower ferritin concentrations. The proposed sequence of physiologic processes leading to the low stores is chronic hypoxia in the fetus and diversion of fetal iron to the bone marrow to support erythropoiesis. The consequence of this diversion to the bone marrow is a diminution of iron available to the

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fetal brain. Differences in iron-dependent functions, including impaired neurodevelopment, electrophysiologic abnormalities, and memory deficits, have been shown between normal term infants and infants of diabetic mothers. Premature infants are also at risk of earlier iron deficiency than term infants, and iron supplements are recommended by ≥ 2 mo of postnatal life (6). This topic was recently reviewed by Georgieff and Innis (7).

Another example of apparent perturbation in fetal transport is suggested by results of zinc supplementation trials, which have shown that SGA infants are particularly susceptible to zinc deficiency. Zinc supplementation of breastfed SGA infants during the first year of life results in improved physical growth (8) and substantially reduced infectious morbidity and mortality (9). A theoretical basis for these observations is provided by observations of the size of the exchangeable zinc pool (EZP) in SGA versus appropriate-for-gestational-age premature infants. The EZP represents metabolically active zinc and is defined as the size of the combined pools that exchange with the zinc in plasma within 3 d (10). For infants of a similar gestational age, we have reported that the EZP size at birth, both absolute and relative to body weight, is significantly smaller in SGA infants (11). In term infants, hepatic metallothionein-bound zinc, which would be a major component of the EZP, is thought to be available for utilization during the first 2–3 postnatal months (12, 13). Hence, the smaller EZP size in the SGA infants suggests that this hepatic zinc would be expended at an earlier postnatal age.

MATERNAL NUTRITIONAL STATUS AND COMPOSITION OF HUMAN MILK

The macronutrient composition of human milk is relatively robust across a range of dietary patterns. Maternal diet has more influence for certain micronutrients, especially vitamins (14). The mineral content of human milk is generally considered to be more resistant to differences in maternal dietary intake. Despite this, it is also clear that there are significant interindividual differences in zinc concentrations in human milk (15, 16). Although understanding of the biology of zinc transporters in the mammary gland has advanced dramatically in recent years (17), the control mechanisms for secretion of zinc into human milk are not yet fully understood, nor are the factors that account for these interindividual differences.

Data have gradually accumulated suggesting that zinc concentrations in human milk are relatively resistant to differences in maternal zinc status and dietary zinc intake. Randomized maternal zinc supplementation trials in well-nourished women have not shown a change in milk zinc concentrations (16, 18). Animal data suggest that adaptation of zinc transporters can maintain milk zinc concentrations with mild zinc depletion but that more moderate deficiency is associated with reduced milk zinc concentrations (19, 20). Randomized controlled trials similar to those in well-nourished women have not been reported for undernourished or zinc-deficient populations, which precludes definitive conclusions about the relation between maternal diet and milk zinc concentrations in such conditions.

Cross-sectional data from diverse populations with a wide range of zinc intakes are somewhat conflicting but overall indicate similar milk zinc concentrations at comparable postpartum stages (Figure 1). For example, rural Chinese lactating women with a mean dietary zinc intake of 7.6 mg/d, or $\approx 75\%$ of the estimated average requirement (EAR) for lactating women (24),

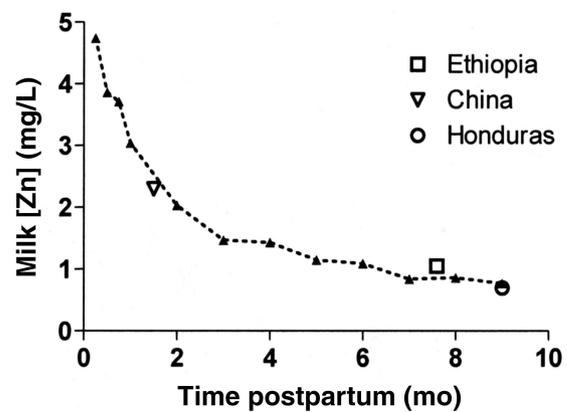


FIGURE 1. Longitudinal human milk zinc concentrations from Denver women (dashed line with filled triangles) (16); other symbols represent cross-sectional data from developing countries as indicated (21–23).

were found to have milk zinc concentrations at 6 wk postpartum that were remarkably close to those of women from Denver, CO (21). Detailed metabolic studies in these same lactating Chinese women indicated that homeostatic adaptation to the low zinc intakes included a greatly enhanced absorption efficiency of dietary zinc, as well as relative conservation of endogenous zinc losses from the intestine (21). A comparison of undernourished and well-nourished women from Honduras and Sweden, respectively, found that milk trace mineral (iron and copper) concentrations at 9 mo postpartum were similar between the 2 study populations. The zinc concentration at 9 mo was slightly higher in the Honduran women and was similar to that at a similar time point in the Denver women (16, 22). We also recently reported that milk zinc concentrations in lactating women in a region of southern Ethiopia with a high prevalence of maternal zinc deficiency were not significantly different from those of well-nourished women (23).

In addition to the independence of milk zinc concentrations on maternal diet, 2 other critical aspects of zinc in human milk have important implications for breastfed infants: the sharp physiologic decline in concentrations over the early months of lactation and the intraindividual tracking of concentrations (16). With respect to the decline in milk zinc concentrations, short-term maternal supplementation trials in both the early weeks postpartum and later months failed to alter the 3–4-fold decline in concentrations between 2 wk and 5 mo (25, 26). The observation of tracking of milk zinc concentrations implies that women who secrete relatively higher amounts of zinc in early lactation will also tend to do so later in lactation (16). Indeed, Umata et al (27) found that Ethiopian infants born to the lowest “zinc secreting” mothers were more stunted than were infants of women with higher zinc concentrations in milk, and milk zinc concentration was one of several factors related to feeding associated with stunting in this population.

INFANT ZINC REQUIREMENTS: INTAKE AND HOMEOSTASIS

Exclusive breastfeeding is considered adequate to meet the nutrient needs of normal term infants for approximately the first 6 mo of life (28, 29). This is achieved for zinc by a combination of a relatively high intake of bioavailable zinc from human milk and the availability of some zinc hepatic stores. For iron, intake



from milk is more modest, and meeting requirements is more dependent on the infant's iron endowment at birth and on the postnatal rate of its expenditure.

Several factors contribute to the dependence of older infants on appropriate complementary foods (or other sources, such as supplements) to meet the requirements of the essential minerals. As described above, these factors include the exhaustion of neonatal stores, the physiologic decline in milk concentrations (most marked for zinc), and the resistance of milk concentrations to maternal intake. Gibson et al (30) have estimated that >90% of the 9–11-mo-old infant's requirements for iron and zinc need to be provided by complementary foods. Others have reached similar conclusions regarding the vulnerability of older breastfed infants in developing countries for deficiencies of iron and zinc with typical complementary feeding practices (31). The recognized importance of these trace elements to normal neurologic development, somatic growth, and immune function underscores the importance of complementary feeding strategies to provide adequate amounts of these nutrients to older infants. The infant's vulnerability to iron deficiency anemia has provided the basis for common recommendations in the United States to use iron-fortified infant cereals as an early complementary foods (32). Recognition of a similar vulnerability to zinc deficiency has not as broadly influenced recommendations and practice.

By using a factorial approach, the Food and Nutrition Board of the Institute of Medicine (21) estimated the physiologic requirement for zinc for 7–12-mo-old infants to be 0.84 mg/d, and the EAR to be 2.5 mg/d (21). In a longitudinal study of infants who were exclusively breastfed (ie, no formula), we reported the zinc intake from complementary foods at 7 mo to be ≈ 0.5 mg Zn/d, with an additional 0.5 mg/d contributed by breast milk, the latter measurement being based on 72-h test-weighing (33). Cross-sectional zinc intake data from complementary foods for a different group of 5–7-mo-old exclusively breastfed infants enrolled in a metabolic study also averaged 0.5 mg/d (34). These data suggest that this is a fairly typical zinc intake for US breastfed infants in the early months of complementary feeding, and thus that usual intakes fall far short of the EAR. Similar intake data are not available for developing countries, but diets based on plant staples for complementary foods are likely to provide intakes in the same range, and, as discussed above, zinc intakes from human milk are also likely similar. Hence, these intake data provide a plausible case for inadequate zinc intake in older breastfed infants.

The potential homeostatic responses of infants to marginal dietary intake include enhanced efficiency of absorption, minimized endogenous losses, and functional accommodation to adjust to the limited supply. Present knowledge suggests that the capacity for breastfed infants' homeostatic adaptation does not preclude the development of deficiencies. If we apply the absorption data derived from stable-isotope studies in breastfed infants, the fractional absorption of zinc from human milk alone is somewhat >0.50 (35). Fractional absorption from typical complementary foods, on the basis of single-meal studies, has been reported to range from ≈ 0.40 to 0.50 (34, 36). Such relatively favorable fractional absorption figures, however, mislead without clear linkage to the amount of actual absorbed zinc. With a test meal of infant cereal, we reported the amount of absorbed zinc in 7-mo-old breastfed infants to be extremely modest at <0.1 mg (36). There was no evidence of compensation for a habitually low intake (and possible marginal zinc status) by a

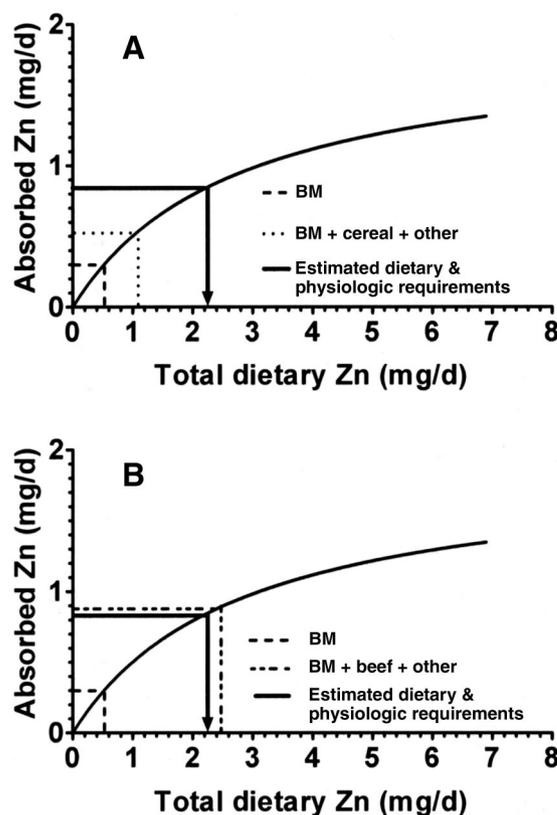


FIGURE 2. Daily total absorbed zinc (TAZ) versus daily total dietary zinc (TDZ) for 7-mo-old infants. The data were fit with a basic saturation response model (solid line) described by the equation $TAZ = (A_{max} \times TDZ)/(IA_{50} + TDZ)$, where A_{max} is the maximal absorption of zinc and IA_{50} is the quantity of zinc intake required for half-maximal absorption (40). Horizontal lines from these intercepts give the corresponding quantity of zinc absorbed on the y axis. The intercept of the line from the y axis for the physiologic requirement for older infants estimated by the Food and Nutrition Board (21) with the model gives the estimated dietary requirement. A: Measured intakes of zinc from breast milk (BM), infant cereal, and other plant-based complementary foods. B: Measured intakes of zinc from BM, pureed meat (beef), and other complementary foods.

high absorption efficiency, although the presence of phytate in the cereal may have affected the infants' ability to absorb a larger fraction of the ingested zinc. In contrast, although the fractional absorption of zinc from pureed meat was not significantly different from that from the cereal, the average amount absorbed, 0.17 mg, was several-fold higher because of the much higher zinc concentration in the meat (36).

Although single-meal studies can provide comparisons of the efficiency of absorption of zinc from those test meals, studies of zinc homeostasis designed to estimate zinc requirements and for other purposes require measurements of total intake and absorption of zinc for an entire day. Absorption of zinc by the enterocyte is a saturable, active process (37), and total absorption of zinc each day is most appropriately compared with total intake of zinc by means of saturation response modeling (38–40). The saturation response models depicted in **Figure 2** (individual means not included) are derived from mean data for all total diet infant studies (38). The age of these infants averaged ≈ 4 mo, and by 7 mo, it is expected that this model would show a close but slightly steeper curve. This model demonstrates the higher efficiency of zinc absorption the lower the intake. At the lowest intakes, zinc

transport is fully up-regulated, which is the principal explanation for the relatively favorable fractional absorption of zinc from breast milk and any low-zinc food. At higher zinc intakes, the efficiency of zinc absorption progressively decreases as absorption is down-regulated. Despite the down-regulation, the total daily quantity of zinc absorbed increases with increasing zinc intake up to a maximum for that age (≈ 2 mg/d for term infants). This modeling has been used to estimate the total quantity of zinc absorbed each day by 7-mo-old infants from the different diets in our study of introducing meat as the first complementary food (41, 42). The very limited absorption of zinc from breast milk and ad libitum feeding of infant cereal for 1 d even when intake of other sources of zinc are included is estimated in Figure 2A. The contrast when beef is offered is shown in Figure 2B, in which case both physiologic and dietary zinc requirements are met.

Endogenous losses, particularly those from the gastrointestinal tract, provide the other critical aspect of zinc homeostasis. Data for intestinal zinc losses are unavailable for infants consuming mixed diets; data available from exclusively breastfed or formula-fed infants indicate a positive correlation between daily absorbed zinc and endogenous fecal zinc excretion (43). The normal young breastfed infant relies on the combination of excellent absorption efficiency and conservation of intestinal endogenous zinc to maintain adequate zinc retention for growth (35). With the very modest daily absorbed zinc by older breastfed infants consuming plant-based diets, the intestinal endogenous losses would thus be predicted to be minimized under normal circumstances. The extent to which this occurs, however, with consumption of complementary foods has not yet been examined. Host factors, such as episodes of diarrhea, would increase gastrointestinal losses and would thus predispose to deficits (44).

ZINC AND IRON DEFICIENCY IN OLDER BREASTFED INFANTS

Beyond the theoretical risks posed by a zinc intake that is low relative to the EAR for older breastfed infants and toddlers, a pertinent question is whether there is evidence of deficiency in this population. The results of randomized controlled trials of zinc supplementation of infants and young children have left little doubt that zinc deficiency is common in young children in developing countries (45). The findings of reduced morbidity from diarrhea and pneumonia in particular, 2 of the major causes of childhood mortality, undoubtedly have substantially contributed to the identification of zinc supplementation as an important strategy to prevent deaths in young children (1). Several large-scale zinc supplementation trials included infants and children between 6 mo and 3 y of age, without specifically targeting older infants (45). The results of trials of zinc supplementation of term breastfed infants aged < 6 mo, however, have been inconsistent and generally have not shown benefit, especially for those with birth weights appropriate for gestational age (46–48). These observations support the general adequacy of exclusive breastfeeding for ≈ 6 mo.

One published zinc supplementation trial in Ethiopia specifically targeted older breastfed infants who were also receiving the local customary complementary foods, which included primarily the dietary staples of cereal grains and starchy root (49). In this study, zinc supplements were initiated at 6 mo of age and were continued through 12 mo in a randomized, double-blind design. Infants were also stratified according to the presence or absence

of stunting, which was highly prevalent in the population. Results included significant improvements with zinc supplementation in both linear and ponderal growth, and significantly reduced morbidity from infections. Benefits were greater for all outcome variables for the infants who were stunted at the outset. These results strongly suggest an underlying deficiency.

Documentation of widespread iron deficiency in infants and young children is clear. Some data suggest a prevalence of anemia (hemoglobin < 100 g/L) of one-half to three-quarters of infant and child populations in developing countries; substantial numbers were also reported to have moderately severe anemia as well (50). Randomized trials of iron supplementation have convincingly shown benefits in motor and language development in vulnerable populations (51, 52).

In the United States, where the prevalence of breastfeeding without formula feeding is much lower than in many developing countries, current survey data indicate that $\approx 10\%$ of all US infants, equivalent to $\approx 400,000$ infants, are “exclusively” breastfed (ie, no formula but with introduction of complementary foods) through 12 mo (53). Few intervention studies have addressed zinc status in older breastfed infants in developed countries. Evaluation of zinc and iron status in Denver breastfed infants at 9 mo indicated that about one-third of the all of the infants had plasma zinc and ferritin concentrations below recommended cut-offs, which suggests marginal status for these 2 trace minerals (42). More complete characterization of the zinc status of this group of infants in developed countries will depend on randomized controlled trials of zinc supplementation with functional outcomes, such as somatic growth, appropriately sensitive and targeted indexes of neurocognitive development, and biomarkers of status.

CURRENT RECOMMENDATIONS AND PRACTICES FOR COMPLEMENTARY FEEDING

The World Health Organization (WHO) and the Pan American Health Organization (PAHO) have published guidelines for complementary feeding, which emphasize both nutrition and food safety issues (54). The guidelines emphasize the importance of continued breastfeeding after 6 mo of exclusive breastfeeding, of safe (hygienic) preparation and storage, of the use of thick gruels rather than watery soups, of offering complementary foods several times during the day, and of providing a variety of different foods. Relevant to this review, the guidelines also specifically note that “meat, poultry, fish or eggs should be eaten daily, or as often as possible” (54). Additionally, the report notes that plant-based foods alone are inadequate to meet micronutrient requirements without the use of supplements or the nutrient fortification of staple foods (54). As discussed in recent reviews, typical current feeding practices in developing countries include the use of cereal gruels and very modest amounts of meats (31, 50). Recent studies have shown a benefit of meat consumption on nutritional status in developing countries (55–57).

Contemporary recommendations in the United States have been much less explicit than the international guidelines regarding the emphasis on flesh foods for older infants, although several reports have suggested meats as an alternative or complement to iron-fortified infant cereal (58, 59). The American Academy of Pediatrics notes that meats can be offered to infants as an early complementary food but does not specifically recommend this practice for breastfed infants, for whom it is most important from



a nutritional standpoint (14, 32). Most recently, the Institute of Medicine's report on the food package for the Special Supplemental Food Program for Women, Infants, and Children proposed that meat should be provided as part of the food package for breastfed infants at 6 mo of age (60).

Limited data are available on the actual dietary intakes of infants in the United States. A large survey of dietary practices of infants and toddlers found that most 7–11-mo-old infants consumed infant cereals, fruit, and vegetables, but <10% consumed meats or poultry as single foods (61). More common was consumption of mixed dinners, which are considerably lower in zinc and iron. The survey did not distinguish intakes specifically by formula-fed or breastfed infants; overall, 26% of the infants in the survey were breastfed. These practices for complementary foods are unlikely to pose any risk for formula-fed infants, for whom the risk of micronutrient deficiencies is low. For breastfed infants, however, the intakes of certain micronutrients, including especially zinc, are likely to be substantially below the EAR, given the reported patterns of complementary food choices. Although some brands of infant cereal are now fortified with zinc as well as iron, this is not a universal practice, and no studies have been reported that examine the bioavailability or adequacy of the fortified products.

STRATEGIES TO MEET MICRONUTRIENT NEEDS WITH COMPLEMENTARY FOODS

A comprehensive review of these strategies is beyond the scope of this article but is available in current literature (62, 63). The recognition of the risk of micronutrient deficiencies in older breastfed infants in developing countries has led to consideration of several intervention strategies, including food fortification, micronutrient supplements, and sprinkles. In developed countries, food fortification has been the primary method used to meet the micronutrient requirements of infants. In fact, because most infants in the United States are now formula-fed, the predominance of iron-fortified formula has vastly reduced the risk of iron deficiency in older term infants. Meeting the relatively high nutrient needs of young children is challenging if reliance is on fortification programs for the entire population. The density of fortification appropriate for adult consumption is unlikely to be realistic for young children. Iron fortification of foods specifically targeted to young children has met with more success in a variety of settings, with documented improvements in growth and rates of anemia (50).

Sprinkles have been shown to be effective in reducing iron deficiency anemia in older infants in developing countries (64), but data are more limited for other micronutrients (65). Iron supplements for older infants are national policy in some developing countries, but recommendations for zinc supplements are limited to treatment of diarrhea (66). Reliance on supplements (eg, iron and zinc) as a strategy poses challenges of distribution and sustainability from a programmatic viewpoint. From a physiologic and nutritional standpoint, the potential for nutrient interactions is more than theoretical (67) and may also be complicated by host factors (68).

Affordability and sustainability are important challenges for any of these strategies. This is especially true for the millions of rural poor, eg, in sub-Saharan Africa, the Indian subcontinent, China, southeast Asia, and other areas. Recognition of these challenges, which are not readily soluble, is leading to expanding

interest in improving complementary feeding from locally produced unfortified foods. As described above in the PAHO/WHO recommendations, emphasis has been on adequate food diversity, including the greater use of animal source foods. Success with introducing these foods has been achieved, eg, with educational strategies in China (69) and Peru (56). Typically, strategies will need to emphasize behavior change communication if success is to be achieved (70).

Currently, the early introduction (at or shortly after 6 mo of age) and regular use of meat is the only effective food-based strategy for providing adequate zinc. That this strategy can be successful in providing adequate zinc was documented in the recent Colorado study alluded to in earlier sections (42). Of note, there were no differences in acceptability or tolerance between the pureed meat and the infant cereal for 6-mo-old infants. Earlier introduction of meats substantially contributes to meeting iron requirements and ensures adequate intakes of vitamins B-6 and B-12. It is of historical interest that in earlier centuries, meat was commonly prechewed and offered to infants as a weaning food, and as recently as 1950, meats were introduced within the first month of life (71). Reviews of complementary feeding practices over time indicate that recommendations for food choices and the sequence of introduction have generally not been evidence based. The challenges of providing meat as an early complementary food are often viewed as insurmountable. The strong rationale for potential benefits and the examples of successful interventions, however, provide potent incentives to pursue broader implementation programs, with concurrent rigorous evaluation of both efficacy and effectiveness.

SUMMARY

Exclusive breastfeeding for the first 6 mo of life followed by optimal complementary feeding are critical public health measures to reduce and prevent morbidity and mortality in young children. The micronutrient needs of younger infants, particularly for iron and zinc, are affected by clinical factors such as birth weight, prematurity, and illnesses. Maternal diet and nutritional status do not have a strong effect on the mineral content of human milk, but the physiologic changes in milk and infants' status determine the dependence of the infant on complementary foods in addition to human milk to meet iron and zinc requirements after 6 mo. The nature of zinc absorption, which is suitably characterized by saturation response modeling, dictates that diets based on foods with a low zinc content (including cereal grains and legumes as well as human milk) are associated with high absorption efficiency but low absolute daily absorbed zinc. Foods with a higher zinc content, such as meats, are associated with lower absorption efficiency but greater absorbed zinc, which, along with human milk and other foods, is sufficient to meet dietary requirements. Current plant-based complementary feeding patterns for older fully breastfed infants in both developed and developing countries pose a strong risk of zinc deficiency. Among the strategies to meet the micronutrient requirements of older breastfed infants, inclusion of meat as an early complementary food should be encouraged, along with fostering the cultural, economic, and social factors that may facilitate and sustain such a fundamental change in current complementary feeding practices.



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