Advancing from Infancy to Toddlerhood through Food

Abstract
Establishing dietary recommendations for micronutrients in young children is difficult. Techniques used to evaluate nutrient intake and bioavailability are hard to apply in this age group. Additionally, large variations in growth rates, dietary patterns, and nutrient losses in early childhood make determinations of dietary requirements difficult. Most recent studies have utilized stable isotopes to determine mineral absorption for iron, zinc, calcium, and magnesium. Vitamin D requirements have been established based on the dietary intake required to maintain a presumed adequate serum 25-hydroxyvitamin D concentration. Comparisons of nutrient requirements established using factorial methods involving absorption determinations and usual population intake are important to identify nutrients of concern related to deficient or excess intakes. Generally, in the USA, the intakes of calcium and magnesium are adequate to meet requirements in most toddler diets which include a milk source or a mineral-fortified milk alternative. Zinc and iron intakes can be below requirements in a substantial proportion of toddlers throughout the world, especially those with minimal meat consumption. Dietary vitamin D is generally below dietary recommendations, but clearly deficient serum 25-hydroxyvitamin D concentrations are less common, and the global role for routine vitamin D supplementation or fortification of the diet remains uncertain.

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Introduction

Children 1–3 years of age (henceforth referred to by the imprecise, but commonly used term “toddler”) are among the most nutritionally understudied population. Techniques to assess micronutrients used in both younger and older age groups, including blood levels, mass balance studies, and isotopic techniques, are extremely difficult to apply to an age group that cannot directly consent to these procedures. It can be difficult to have families or regulatory oversight committees agree to what are perceived to be invasive research protocols with no direct benefit for the healthy children involved in them.

As such, data are very limited, and often only 1 or 2 studies in the last 30 years or more are available to directly evaluate this population. This is unfortunate as this is an age of important neurocognitive and motor development, and nutrient adequacy is critical. Most recent studies, especially of minerals, have used stable isotopes to assess nutrient absorption and metabolism. These techniques are safe although blood drawing and intravenous tracer infusions are not entirely non-invasive [1]. However, some important minerals in this age group, such as phosphorus, do not have minor stable isotopes that can be used as tracers, and others, including many vitamins, have poorly defined endpoints for nutritional adequacy or excess.

In this report, nutrient requirements of key micronutrients needed for growth and development of toddlers will be discussed. These are iron and zinc, critically needed for neurodevelopment, growth, and immune functioning, and calcium, vitamin D, and magnesium, related primarily to bone health. We will evaluate the current dietary recommendations for these nutrients, how these were determined, and how they relate to estimates of usual nutrient intake.

Methods to Assess Micronutrient Requirements

For the minerals, the technique most widely used in recent decades has been the factorial method in which nutrient needs for growth and recovery of losses are compared to intake-adjusted bioavailability using stable isotopes. For calcium, data for growth requirements are derived from relatively recent bone mineral content studies, but for most minerals growth needs were calculated based on very limited data from cadaver studies primarily performed in the first half of the 20th century.

For iron, the stable isotope methodology of determining absorption, derived from earlier radioactive isotope techniques, relies on the incorporation of an
orally administered iron isotope (often given with an enhancer of iron absorption such as vitamin C or with a meal) in red blood cells at 14–28 days [2, 3]. Interpretation of these findings includes evaluation both of the iron source and the relationship between the iron intake and the iron status, frequently assessed using serum ferritin, of the child. This technique is well described and has the benefit of being relatively easily adapted to research settings throughout the world.

For zinc, calcium, and magnesium, the preferred mineral absorption technique is the dual tracer study in which one stable isotope is administered orally, and a different one is given intravenously with primary analysis of absorption based on the relative enrichment of recovered isotopes in the urine [4–6]. This technique is more challenging for use in toddlers due to the difficulty both in administering the isotope intravenously and in collecting multiple or extended urine specimens. Nonetheless, some studies have been performed although further data are critically needed, especially in nonindustrialized nations. A significant ongoing limitation to further expansion of this research is the cost of the isotopes themselves as well as the cost and limited availability of sites capable of accurate analysis of biological samples enriched in mineral-stable isotopes.

Assessing usual nutrient intake to determine the relationship between identified nutrient intake requirements and usual population intakes is also challenging in toddlers. The diet in this age group is often highly variable. It is not simple to have parents accurately recall or measure dietary intake, and no real nutritional steady state is generally feasible prior to conducting short-term isotopic absorption studies. Fortunately, with these limitations in mind, in addition to the National Health and Nutrition Examination Survey (NHANES), there are multiple datasets available recently in the USA and throughout the world that can be used to assess usual intake, although, as with absorption studies, more data are needed from nonindustrialized countries [7–12].

These data limitations are important in interpreting dietary recommendations [13–16]. It is not reasonable to be overprecise in interpreting recommendations and their relationship with usual intakes of populations of toddlers. Analysis of the proportion of the population below or above a threshold is often an inadequate way to determine nutrient adequacy in the face of severe limitations in the precision and accuracy of the data. Disease-oriented outcomes, including rickets for example, reflect extremely deficient outcomes in most cases and are often unreliable markers of population nutrient adequacy.
Specific Nutrients

Iron

The recommended intakes for iron have been set using a factorial approach in which the mean requirement of toddlers is about 0.6 mg/day of absorbed iron and the 97th percentile of this requirement is 1.2 mg/day. Of note is that about 60% of the requirement is related to basal iron losses – not growth needs for new red blood cell production (Fig. 1). The Institute of Medicine then used an approximate absorption fraction of 18% to calculate an estimated average requirement (EAR) for iron of 3 mg/day and a recommended dietary allowance (RDA) of 7 mg/day [13]. These values are relatively similar to those determined by the European Food Safety Authority (EFSA) of 5 and 7 mg/day, respectively, for the equivalent requirements [16].

In comparing these values to usual intakes on a global basis, it appears that the mean daily intake of iron in the USA, Mexico, Europe, and Australia is about 7–10 mg consistent with most children in these locations having intakes above the EAR [7–10, 12]. In contrast, lower daily intake with a mean of about 5 mg was reported in the Philippines [11]. In the USA, about one-fourth of toddlers have an intake below the RDA suggesting that there remains a subset of toddlers in whom further efforts to ensure adequate intake is indicated [8].

Of concern is that, globally, the prevalence of anemia remains very high with large differences between regions, ranging from about 20 to nearly 70%. Assuming that 30–50% of this anemia is related to iron deficiency, it may be that the factorial calculation used to determine dietary recommendations underestimates the biological need in this population [17, 18]. If this is the case, both higher basal iron loss rates and lower bioavailability from typical diets than the 18% used to calculate the dietary reference intake values are likely responsible.
When we evaluated iron bioavailability in a population of small children in Mexico, we found huge variability in absorption efficiency depending on the iron compound and whether it was provided with vitamin C [3]. This range in absorption (from 1 to 24% of intake) highlights the need to focus not just on usual population daily intakes for iron but also on the iron source and other dietary components.

**Zinc**

Consideration of zinc requirements has focused both on the RDA but also on the limits of intake, referred to as the tolerable upper limit (UL). The EAR for zinc has been set as 2.5 mg/day in the USA/Canada and the equivalent value of 3.6 mg/day in Europe [13, 15]. The RDA for zinc has been set for this age group at 3 mg/day in the USA/Canada and 4.3 mg/day for Europe [13, 15]. Our studies in this population using stable isotopes tend to support the EFSA value for average requirement although it is difficult to be precise as relatively few toddlers have these very low iron intakes in the USA [5]. Regardless of the exact EAR recommended, the EAR is well below the usual intakes in the USA, Canada, and Mexico of about 6–8 mg/day [7, 8].

This usual intake level has prompted concerns as the USA and Canada UL is 7 mg/day, implying that a large proportion of toddlers may have high zinc intakes leading to a risk of toxicity, potentially related to a diminished copper status [13]. Numerous groups have challenged this UL as not reflective of dietary sources of zinc and copper, and recently the izincg collaborate has suggested that a no adverse effect level of 10 mg/day in toddlers 1–3 years old is more appropriate [19], and the World Health Organization (WHO) sets a UL value of 23 mg/day [20]. There is little if any evidence that usual diets including high-zinc-containing natural dietary sources, such as red meat, lead to deficiencies in other

<table>
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<tr>
<th>Table 1. Summary of key current considerations: iron and zinc</th>
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<tr>
<td><strong>Iron</strong></td>
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<td><strong>Zinc</strong></td>
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micronutrients, although concern may exist when the zinc is taken as a supplement (Table 1) [21].

**Calcium**
Calcium dietary requirements have largely been set in childhood based on the usual rate at which the skeleton accretes calcium. Various estimates based largely on bone mineral mass accumulation data suggest this rate in toddlers is about 100 mg/day on average with a high end (97th percentile value) of about 140 mg/day. The EAR in the USA and Canada is 500 mg/day, and the RDA is 700 mg/day in this age group [22]. These values are consistent with a stable isotope study we conducted in toddlers evaluating calcium absorption and retention on a range of calcium intakes from about 100–1,000 mg/day [4].

Usual calcium intakes in the USA and Canada are above both the EAR and the RDA at about 950 mg/day although up to 20% of toddlers will be below the RDA [7, 8, 14]. This provides support for provision of high-calcium-containing dietary sources in this age group, with yogurts or similar foods containing naturally high calcium being considered for those toddlers whose primary non-water beverage source is breast milk or a non-calcium-fortified plant beverage (Table 2).

**Vitamin D**
It is impossible to consider dietary calcium requirements without consideration of vitamin D requirements, and these were considered together in the dietary reference intake process published by the Institute of Medicine in 2011 [14]. Although a full review of vitamin D needs of toddlers is beyond the scope of this

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**Table 2. Approximate calcium content of typical beverages for toddlers**

<table>
<thead>
<tr>
<th>Beverage</th>
<th>Calcium concentration</th>
<th>Daily intake, per 500 mL/day</th>
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<tbody>
<tr>
<td>Breast milk</td>
<td>26 mg/100 mL</td>
<td>130 mg</td>
</tr>
<tr>
<td>Whole cow’s milk</td>
<td>120 mg/100 mL</td>
<td>600 mg</td>
</tr>
<tr>
<td>Fortified rice/soy/almond milk¹</td>
<td>20 mg/100 mL</td>
<td>600 mg</td>
</tr>
<tr>
<td>Toddler “formula”²</td>
<td>110 mg/100 mL</td>
<td>550 mg</td>
</tr>
<tr>
<td>Goat milk</td>
<td>130 mg/100 mL</td>
<td>650 mg</td>
</tr>
<tr>
<td>Unfortified almond milk¹</td>
<td>&lt;10 mg</td>
<td>&lt;10 mg</td>
</tr>
<tr>
<td>Unfortified soy milk¹</td>
<td>25 mg</td>
<td>125 mg</td>
</tr>
</tbody>
</table>

¹ Many, but not all, soy- and other plant-based beverages commercially sold are calcium fortified.
² The World Health Organization and American Academy of Pediatrics do not recommend the use of these formulas.
review, a few key points are relevant. First, the outcome usually used to evaluate vitamin D status, the serum 25-hydroxyvitamin D (25-OHD) concentration, is not a full measure of the most clinically relevant outcome in toddlers preventing nutritional rickets. The complex relationship between calcium and vitamin D deficiency leading to rickets has been discussed in detail in several reviews [23, 24]. Although targeted levels of 25-OHD are usually set at 50 nmol/L, it is likely that calcium absorption is only substantially limited at lower levels, such as below 30 nmol/L [24, 25]. Whether other potential benefits, such as immune function, require higher 25-OHD levels remains uncertain, especially in small children.

A globally based approach to decreasing vitamin D deficiency has recently been published. Key issues are the use of national strategies related to food fortification and/or supplementation strategies with vitamin D. These may be best considered in countries in which 20% of the population at risk has a 25-OHD level below 30 nmol/L and/or a >1% prevalence of rickets [24]. This is consistent with a Cochrane review suggesting that supplementation of deficient children (approximately <35 nmol/L) may be useful, but that there are few data supporting supplementation strategies to improve bone density in healthy children with higher 25-OHD levels [26]. In the USA, <20% of the population has a 25-OHD level <50 nmol/L, and in Mexico a recent study found 25% <50 nmol/L [27]. Nonetheless, the persistence of clinical rickets in many parts of the world is consistent with careful vigilance, and there is little likelihood of harm in vitamin D fortification strategies for milk and other beverages.

Magnesium
The importance of magnesium for health outcomes is increasingly recognized in all age groups. However, although stable isotopic absorption studies are feasible for magnesium, they are technically more difficult than for calcium and zinc, and they have been very rarely performed in children. Furthermore, because toddlers only retain a very small amount of magnesium daily (about 10–20 mg), it is difficult to be precise about the relationship between dietary magnesium intake and net retention.

With these limitations in mind, we found that a dietary intake of about 100 mg/daily led to a net magnesium retention of about 20 mg/daily in toddlers. However, it is likely that 20 mg/day slightly exceeds the average typical magnesium retention in this age group. The EAR for magnesium was set at 65 mg and the RDA at 80 mg/day [28]. Although these values may be a bit low, it is important to note that the 1st percentile of usual magnesium intakes in the USA and Canada is 80 mg/day, and the median intake is 180 mg/day. These data suggest limited population-based concern in the USA related to magnesium dietary suf-
ficiency, but further information would be needed on a global basis or related to the bioavailability of different magnesium sources. Of note is that in slightly older, i.e., 4- to 8-year-old children, we found a closer relationship between dietary magnesium intake than dietary calcium intake for total body bone mineral content and density, further providing evidence that a closer look at the role of magnesium in bone health in small children should be undertaken (Table 3) [29].

### Dietary Sources of Key Minerals and Fortification Strategies

The diet of toddlers is unique in that it represents a transition between that of infants, which is largely based on breast milk or formula with gradual introduction of solid foods, and that of older children, which at the end of the toddler age period begins to resemble the family diet.

With regard to minerals, in many countries, a key source of bone minerals and vitamins, including calcium, magnesium, and vitamin D, is cow’s milk, or for families who do not use cow’s milk, soy or other plant milks. Cow’s milk is rich in these components and represents the major mineral source for them. Soy and other non-cow milks are often fortified with minerals to meet these needs. For toddlers who do not receive significant cow’s milk or fortified plant milks, including those infants who are breastfed during the toddler age period, bone minerals, and especially vitamin D, may be minimal, and there may be some risk of rickets. In these cases, it is generally recommended to provide vitamin D via

| **Table 3. Summary of key current considerations: bone minerals and vitamin D** |
|---------------------------------|---------------------------------|
| **Calcium**                     | Likely average physiological need about 300–400 mg/day  |
|                                 | Easily achieved with diet that includes dairy or fortified plant or other beverages |
|                                 | Breastfed toddlers should have adequate solid food or other dietary source of calcium |
|                                 | Need to have awareness of this issue especially in vegan or other restrictive diets |
| **Vitamin D**                   | Related to bone health, there is a low but definite persistence of severe vitamin D deficiency in this age group, since dietary intakes are low in many populations |
|                                 | Specific risk groups exist, and rickets remains a clinical problem especially when combined with low calcium intakes |
|                                 | Global strategies and assessments are needed to evaluate the need for fortification and supplementation |
| **Magnesium**                   | No good biomarker exists for magnesium |
|                                 | Limited accretion data suggest target retention of 10–20 mg/day in childhood |
|                                 | Magnesium-deficient intake is likely relatively uncommon with mixed diets, but difficult for clinicians to assess |
|                                 | No current recommendations for routine fortification or supplementation, but limited data available |
supplement. Calcium is less commonly given via supplement but is found in foods, such as corn tortillas prepared from lime treatment. We evaluated calcium absorption from these tortillas with stable isotopes and found a high rate of absorption [30]. Generally, calcium is less likely to be fortified in foods such as flour than other minerals, but this can be done in high-risk populations, or supplements can be provided where the rate of rickets related to mineral deficiency is substantial. Attention needs to be paid related to other components of the diet including levels of phytates, which may affect calcium absorption as well as that of other minerals [31].

Dietary iron sources including fortified foods are a critical issue especially in populations with high rates of iron deficiency. A detailed review of this topic is beyond the scope of this review, but a critical issue as noted above is the form of the iron provided and its bioavailability. The diet of toddlers is often very low in meat, and fortification of grains is therefore widely done both for iron and zinc. Critical issues also include the iron:zinc ratio in the fortificants and the specific method of preparation of the fortified food. Of importance is that when fortification strategies do not include a careful evaluation of iron bioavailability, they may not achieve desired results [3, 32]. Nonetheless, fortification strategies remain a central pillar of nutritional programming in many countries related to the iron needs of toddlers.

**Future Research Needs**

Determination of dietary requirements for vitamins and minerals in small children requires accurate evaluation of usual intakes, mineral absorption efficiency, and excretion along with an assessment of an outcome measure that is biologically meaningful. The lack of adequate data in this age group for each of these should be addressed with specific research targeting this population. This effort needs to be global in scope and to fully account for differences in dietary patterns that are regional or cultural in nature. Overemphasis on very specific values for dietary recommendations may lead to unnecessary interventions, and the risks and benefits of nutrient supplementation and fortification strategies need to be assessed broadly.

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Conflict of Interest Statement

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References


