Nutritional Causes of Linear Growth Failure During Complementary Feeding

Rosalind S. Gibson and Christine Hotz

Department of Human Nutrition, University of Otago, Dunedin, New Zealand

In developing countries, the prevalence of linear growth faltering increases rapidly among infants and children, sometimes beginning soon after birth (1) but generally between 6 and 18 months of age, coinciding with the period of complementary feeding and the childhood growth phase (2). The period of complementary feeding is defined as the time when any nutrient-containing foods or liquids are offered to young children in addition to breast milk (3). By about 6 months of age, breast milk alone is no longer sufficient to support normal growth of full-term infants (3). Hence, at this time, the nutritional adequacy of complementary foods becomes critical to support the childhood growth phase (3).

The reason for linear growth faltering during infancy is not exactly known; it probably arises from multiple causes such as the effect of maternal malnutrition on fetal growth, alterations in fetal psychosocial conditions, frequent infections, and poor dietary intakes. When these adverse conditions are multiple or chronic, interruptions in normal growth accumulate, resulting in an increased prevalence and severity of stunted growth and disturbances in development. Unfortunately, these adverse outcomes often persist into later childhood when they have been associated with delays in cognitive development and behavioral abnormalities (4,5) as well as increased risk of morbidity and mortality (6,7).

Poor dietary intakes during complementary feeding are associated with deficits in the quality as well as the quantity of complementary foods (8). In developing countries, infants may receive insufficient amounts of complementary foods and thus inadequate intakes of energy because of their limited gastric capacity, poor child feeding behaviors, anorexia induced by infections, and food shortages. Furthermore, the complementary foods offered to the infant are often plant based, with a low proportion of energy from animal products. Hence, they have a low content and bioavailability of nutrients, many of which play a role in linear growth. Such complementary foods are said to have a poor dietary quality (3,9). The nutritional adequacy of complementary foods can be assessed by comparison with the recent estimates of energy and nutrient needs from complementary foods for infants of various ages (3).
In this review, we focus on the adequacy of the complementary diet to meet the estimated nutrient needs of infants for linear growth. The interaction of nutrition with infection during complementary feeding is not discussed. For each growth-limiting nutrient, we summarize the mechanism and evidence for its role as a determinant of linear growth, based on observational and intervention studies. Next, we discuss the role of multiple micronutrient deficiencies in linear growth failure during complementary feeding, with reference to the use of multiple micronutrient supplements, fortificants, or micronutrient-rich foods to enhance the dietary quality of complementary foods. Again, both observational and intervention trials are reviewed in this section. Finally, we summarize briefly some possible strategies at the household and commercial levels for improving the nutritional adequacy of complementary foods in developing countries, followed by an outline of future research activities.

THE ADEQUACY OF GROWTH-LIMITING NUTRIENTS IN THE COMPLEMENTARY DIET

Under normal conditions, breast milk alone is adequate to meet the energy and nutrient requirements and support normal linear growth for the first 6 months of life (10,11). However, some circumstances prevent normal linear growth with exclusive breast-feeding during this period. These include cases when the in utero accumulation of nutrients is poor or the volume and nutrient composition of breast milk are compromised, although the latter situation is less likely to be a major cause of early growth faltering (3) unless accompanied by severe maternal malnutrition (12).

At around 6 months of age, the supply of energy and certain nutrients from breast milk is no longer adequate to meet the nutritional requirements, and so the balance of requirements must be provided by a source of nutritionally adequate and hygienically prepared complementary foods. Introduction of complementary foods before this time has been associated with poor linear growth in developing countries (11), probably mediated through an increased risk of diarrheal infection (13,14) and deficits in the quality and quantity of the foods offered together with some displacement of breast milk. When the latter occurs, the intake and bioavailability of growth-limiting nutrients become even more compromised, especially if the complementary foods are consumed together with breast milk (15,16). In the following discussion, we will focus only on the adequacy of the complementary diet to support linear growth from 6 months of age.

Recently, the World Health Organization (WHO) (3) has calculated the energy and nutrients needed from complementary foods for infants of various ages in developing countries. These theoretical energy and nutrient needs are based on the difference between the age-specific energy and nutrient requirements and the energy and nutrients provided by breast milk, taking into account the volume and composition of breast milk consumed. The estimated needs have been compiled for low, average, and high intakes of breast milk, corresponding to mean - 2 SD, mean, and mean + 2 SD, respectively. Only the estimated needs for energy and selected growth-limiting nutrients are shown in Table 1. Values for the nutrient composition of mature human
TABLE 1. Estimated needs of selected growth-limiting nutrients from complementary foods by average breast milk intake for infants of various ages

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>6–8 mo</th>
<th>9–11 mo</th>
<th>12–23 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (g/d)</td>
<td>2</td>
<td>3.1</td>
<td>5</td>
</tr>
<tr>
<td>Vitamin A (µg RE/d)</td>
<td>13</td>
<td>42</td>
<td>126</td>
</tr>
<tr>
<td>Riboflavin (mg/d)</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Vitamin D (µg/d)</td>
<td>6.6</td>
<td>6.7</td>
<td>6.7</td>
</tr>
<tr>
<td>Calcium (mg/d)</td>
<td>336</td>
<td>353</td>
<td>186</td>
</tr>
<tr>
<td>Iodine (µg/d)</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Iron low bioavailability (mg/d)</td>
<td>20.8</td>
<td>20.8</td>
<td>11.8</td>
</tr>
<tr>
<td>Iron med. bioavailability (mg/d)</td>
<td>10.8</td>
<td>10.8</td>
<td>5.8</td>
</tr>
<tr>
<td>Iron high bioavailability (mg/d)</td>
<td>6.8</td>
<td>6.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Phosphorus (mg/d)</td>
<td>306</td>
<td>314</td>
<td>193</td>
</tr>
<tr>
<td>Zinc (mg/d)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.2</td>
<td>4.3</td>
<td>5.8</td>
</tr>
<tr>
<td>Zinc (mg/d)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.2</td>
<td>2.3</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Note that data for low (that is, mean -2 SD) and high (mean +2 SD) intakes of breast milk are not shown here but are given in the original reference. RE, retinol equivalent.

<sup>a</sup>Based on the amount of zinc in breast milk from Institute of Medicine (27) and zinc requirements from British dietary reference values (20).

<sup>b</sup>Based on the amount of zinc in breast milk from Krebs NF et al. (45) and estimated zinc requirements using data from Krebs NF & Hambidge KM (21).

Adapted from World Health Organization (3).

Milk (i.e., 21 days postpartum) were derived from the breast milk content from women in industrialized countries, primarily because of the absence of comprehensive data on the nutrient concentrations of breast milk of women in developing countries. A notable exception was vitamin A, for which estimates from measurements in women from developing countries were used (17). In addition, in geographic regions where endemic iodine deficiency exists, it is preferable to use the iodine concentrations for breast milk specific to these regions, where possible, because maternal breast milk concentrations for this trace element are likely to be compromised.

The requirements used to compute these theoretical needs were those compiled by Butte (18) for energy and by Dewey et al. (19) for protein. For all other nutrients, with the exception of zinc, iron, and folate, the UK dietary reference intake (DRI) values (20) were used. The DRI values represent the average requirement plus a factor of 2 SD. For zinc, two estimates were derived: the UK dietary reference value for zinc and another based on the factorial approach using experimental data from Krebs and Hambidge (21) and Krebs et al. (22). The latter estimate is similar to the range for the basal and normative requirement estimates for zinc of high bioavailability published by the WHO (23). For certain nutrients (e.g., manganese), knowledge of the requirements for maintenance and growth is inadequate, and hence manganese has not been included in the following discussion.

These same workers have also compiled desirable nutrient density levels (3), based on the estimates of energy that must be supplied by complementary foods to meet the calculated daily energy requirements for infants aged 6–8, 9–11, and 12–23 months who are receiving low, average, and high intakes of breast milk. Complementary foods with adequate energy and nutrient densities are especially critical in view of the small gastric capacity of infants (around 30 g/kg of body wt) and their relatively large
energy and nutrient requirements per kilogram of body weight. Inadequacies in total intake of complementary foods may occur for a variety of reasons (e.g., caregiver-related feeding behaviors, poor appetite, or the organoleptic quality of complementary foods). Expressing nutrient intakes as a fraction of energy intake allows the identification of those nutrients most limiting in the diet because of inadequacies in total intake of complementary foods per se or in the composition or quality of the complementary diet. In addition, the adequacy of individual complementary foods to meet the estimated nutrient needs can be assessed by this method.

Figure 1 shows the contribution that complementary foods (as a percentage) must provide to meet requirements of growth-limiting nutrients of a child aged 9–11 months, assuming an average composition and intake of breast milk. The figure emphasizes the important role of complementary foods for ensuring that infants of 9–11 months receive their estimated requirements for several essential nutrients known to have a critical role in linear growth (namely, protein, calcium, iron, zinc, riboflavin). For example, complementary foods should provide approximately 25–50% of the estimated need for protein and riboflavin, 60% of calcium, 12% of vitamin A, and 75–100% of the phosphorus, zinc, and iron. Indeed, as much as 98% of the iron and zinc must be provided from complementary foods, even when moderate bioavailability is assumed.

![Diagram showing nutrient contribution](image-url)

**FIG. 1.** Desired contribution of complementary foods as a percentage of the requirements of a child aged 9–11 months consuming breast milk of average volume and composition. Mod B, moderate availability.
Comparison of Actual Nutrient Intakes with Estimated Needs

The ability of weanlings to meet their estimated energy and nutrient needs from complementary foods is challenging, particularly in developing countries where the quantity, quality, and variety of the complementary diet are often limited by the availability of food resources and by traditional infant-feeding practices. Unfortunately, limited comprehensive data are available on the nutrient and antinutrient content of complementary foods used in developing countries and on the actual energy and nutrient intakes of infants derived from complementary foods alone. A summary of the available data on actual intakes of energy and growth-limiting nutrients derived from complementary foods alone from selected geographic regions is given in Table 2 (24–26), where they are compared with the corresponding estimated needs.

These limited comparisons show that intakes from complementary foods fail to meet the estimated needs for iron, zinc, and calcium, when expressed as intakes/day, across all the age groups represented. Such nutrient deficits are typically not affected by poor maternal diet because the latter has little effect on the secretion of any of these nutrients in breast milk (27). Younger infants (6–8 months) are particularly vulnerable to deficits in calcium, iron, zinc, and other nutrients because of their greater nutrient requirements per kilogram of body weight as well as the limited variety and dietary quality of complementary foods typically used for this age group. For

TABLE 2. Actual intakes of energy and linear growth-limiting nutrients derived from complementary foods in various countries and compared with estimated needs

<table>
<thead>
<tr>
<th></th>
<th>Estimated needs</th>
<th>Gambia&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Indonesia&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Malawi&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Zambia&lt;sup&gt;e&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mo)</td>
<td>6–8</td>
<td>7</td>
<td>7–8</td>
<td>6–8</td>
<td>6–9</td>
</tr>
<tr>
<td>n</td>
<td>107</td>
<td>23</td>
<td>46</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>269</td>
<td>NA</td>
<td>174 ± 108</td>
<td>171</td>
<td>197</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>2</td>
<td>NA</td>
<td>3.9 ± 1.9</td>
<td>(105, 311)</td>
<td>(105–390)</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>336</td>
<td>NA</td>
<td>NA</td>
<td>11</td>
<td>28</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>10.8</td>
<td>NA</td>
<td>NA</td>
<td>1.4</td>
<td>(0.6, 2.4)</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>4.2</td>
<td>0.56 ± 0.60</td>
<td>NA</td>
<td>0.9</td>
<td>(1.0–3.2)</td>
</tr>
<tr>
<td>Vitamin A (µg RE)</td>
<td>13</td>
<td>NA</td>
<td>NA</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>Riboflavin (mg)</td>
<td>0.2</td>
<td>NA</td>
<td>NA</td>
<td>0.08</td>
<td>(0.03, 0.13)</td>
</tr>
</tbody>
</table>

Where indicated, values are mean ± SD or median (25th, 75th centiles).
NA, not available; RE, retinol equivalent.
<sup>a</sup>From World Health Organization (3), assuming average breast milk volume and nutrient composition.
<sup>b</sup>From Paul AA et al. (24).
<sup>c</sup>From van Steenbergen WM et al. (25).
<sup>d</sup>Data combined for hungry and harvest season (C Hotz & RS Gibson, unpublished results).
<sup>e</sup>From Hautvast JLA et al. (26).
example, complementary foods with a low viscosity and hence low dry matter content (i.e., 7–10% dry matter) are often used for this age group, resulting in low energy and nutrient densities.

Comparison of Calculated Theoretical Nutrient Intakes with Estimated Needs

In view of the paucity of data on actual energy and nutrient intakes from complementary foods and in an effort to establish whether complementary foods used in a range of developing countries result in similar deficits, theoretical intakes per day (Table 3) and per 100 kcal (Table 4) provided by 23 complementary foods used in parts of Africa, India, Papua New Guinea, the Philippines, and Thailand have been calculated for infants aged 9–11 months and compared with the corresponding estimated needs (28). These theoretical intakes were based on the following assumptions: (a) Infants were receiving three feeds a day as well as breast milk of an average volume and composition; (b) the amount of food consumed per feed was assumed to be 250 g, based on an assumed gastric capacity of 30 g/kg of body wt and the median weight of a well-nourished reference male child aged 10 months (29). Calculated nutrient intakes were based on food composition data compiled by Ferguson et al. (30,31) and Gibson et al. (32) and from other published reports, where necessary.

In general, the nutrient deficits noted for the calculated theoretical intakes from the 23 recipes of complementary foods (Table 3) are comparable with those reported in Table 2. Again, the most notable and consistent nutrient deficits across the range of complementary foods examined were of calcium, iron, and zinc—all nutrients known to have a role in linear growth. These deficits were apparent when intakes were expressed per day (Table 3) and per 100 kcal (Table 4), even if moderate bioavailability for iron and zinc was assumed.

Deficits of other nutrients may also occur in complementary foods based on selected plant-based staples. For example, for those based predominately on unrefined maize, deficits in riboflavin are common, whereas when starchy roots and tubers such as sweet potatoes and cassava and starchy fruits such as bananas (maotoki), and sago (prepared from the starch extracted from the pith of the palm tree, Metrolyxon sagu) form the basis of the complementary diet, protein intakes may also be inadequate. Vitamin A and iodine intakes may be inadequate in infants who consume breast milk, which is poor in these nutrients (3,33). These deficits are particularly important because protein, vitamin A, iodine, and riboflavin are also known to have a direct or indirect influence on linear growth during infancy and childhood.

GROWTH-LIMITING NUTRIENTS IN COMPLEMENTARY DIETS

It is clear that inadequacies in one or more micronutrients may occur in complementary diets used in developing countries. For some of these micronutrients (iron, zinc, riboflavin, vitamin A, and iodine), biochemical or clinical assessment has been used to confirm the existence of such deficiencies during complementary feeding.
TABLE 3. Calculated energy, nutrient, and antinutrient intake per day (assuming 750-g intake) of selected complementary foods

<table>
<thead>
<tr>
<th>Energy (kcal)</th>
<th>Protein (g)</th>
<th>Fat (g)</th>
<th>CHO (g)</th>
<th>B1 (mg)</th>
<th>B2 (mg)</th>
<th>Ca (mg)</th>
<th>Fe (mg)</th>
<th>P (mg)</th>
<th>Zn (mg)</th>
<th>Cu (mg)</th>
<th>DF (mg)</th>
<th>Phy (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maize and wheat-based complementary foods</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17:10:5:68 unrefined maize flour, cow peas, groundnuts, water</td>
<td>869</td>
<td>44</td>
<td>10</td>
<td>155</td>
<td>1.26</td>
<td>0.35</td>
<td>41</td>
<td>8.0</td>
<td>985</td>
<td>5.5</td>
<td>0.95</td>
<td>29.6</td>
</tr>
<tr>
<td>8:2:90 unrefined maize flour, soya flour, water</td>
<td>284</td>
<td>11</td>
<td>6</td>
<td>47</td>
<td>0.29</td>
<td>0.12</td>
<td>36</td>
<td>2.5</td>
<td>331</td>
<td>1.9</td>
<td>0.56</td>
<td>6.2</td>
</tr>
<tr>
<td>22:6:72 unrefined maize flour, soya flour, water</td>
<td>798</td>
<td>32</td>
<td>17</td>
<td>129</td>
<td>0.83</td>
<td>0.34</td>
<td>108</td>
<td>7.2</td>
<td>933</td>
<td>5.4</td>
<td>1.64</td>
<td>17.4</td>
</tr>
<tr>
<td>20:3:4:1:72 unrefined maize flour, soya flour, groundnuts, sorghum, water</td>
<td>786</td>
<td>36</td>
<td>14</td>
<td>130</td>
<td>0.81</td>
<td>0.33</td>
<td>85</td>
<td>6.4</td>
<td>890</td>
<td>5.1</td>
<td>1.20</td>
<td>16.4</td>
</tr>
<tr>
<td>20:6:2:72 unrefined maize flour, groundnuts, sorghum, water</td>
<td>770</td>
<td>35</td>
<td>11</td>
<td>136</td>
<td>0.75</td>
<td>0.30</td>
<td>51</td>
<td>5.5</td>
<td>839</td>
<td>4.7</td>
<td>0.66</td>
<td>15.4</td>
</tr>
<tr>
<td>22:6:72 refined maize flour, soya flour, water</td>
<td>769</td>
<td>30</td>
<td>13</td>
<td>138</td>
<td>0.42</td>
<td>0.18</td>
<td>99</td>
<td>6.4</td>
<td>438</td>
<td>3.1</td>
<td>1.48</td>
<td>8.8</td>
</tr>
<tr>
<td>15:12:3:2:68 wheat, brown sugar, oil sorghum, water</td>
<td>954</td>
<td>16</td>
<td>25</td>
<td>175</td>
<td>0.41</td>
<td>0.10</td>
<td>224</td>
<td>5.9</td>
<td>310</td>
<td>2.5</td>
<td>0.63</td>
<td>8.4</td>
</tr>
<tr>
<td><strong>Rice-based complementary foods</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4:1:7:1:87 rice, kidney beans, roasted sesame, sugar, water</td>
<td>474</td>
<td>14</td>
<td>31</td>
<td>35</td>
<td>0.59</td>
<td>0.12</td>
<td>366</td>
<td>6.8</td>
<td>508</td>
<td>3.5</td>
<td>1.02</td>
<td>6.7</td>
</tr>
<tr>
<td>30:7:4:59 rice, mung beans, ghee, water</td>
<td>1205</td>
<td>31</td>
<td>30</td>
<td>198</td>
<td>0.75</td>
<td>0.25</td>
<td>48</td>
<td>7.7</td>
<td>908</td>
<td>4.8</td>
<td>1.60</td>
<td>10.7</td>
</tr>
<tr>
<td>18:3:12:4:63 rice, sorghum, brown sugar, oil, water</td>
<td>864</td>
<td>22</td>
<td>3</td>
<td>186</td>
<td>0.50</td>
<td>0.15</td>
<td>151</td>
<td>6.3</td>
<td>429</td>
<td>4.7</td>
<td>0.56</td>
<td>10.2</td>
</tr>
<tr>
<td>28:3:1:68 rice, groundnut flour, sugar, water</td>
<td>855</td>
<td>27</td>
<td>6</td>
<td>176</td>
<td>0.67</td>
<td>0.16</td>
<td>28</td>
<td>5.0</td>
<td>787</td>
<td>3.9</td>
<td>1.46</td>
<td>7.0</td>
</tr>
<tr>
<td>20:4:4:72 rice, soya flour, groundnuts, water</td>
<td>781</td>
<td>36</td>
<td>12</td>
<td>134</td>
<td>0.76</td>
<td>0.22</td>
<td>88</td>
<td>5.8</td>
<td>794</td>
<td>4.3</td>
<td>2.02</td>
<td>9.0</td>
</tr>
<tr>
<td>20:4:4:72 rice, soya, sesame, water</td>
<td>845</td>
<td>28</td>
<td>27</td>
<td>123</td>
<td>0.88</td>
<td>0.21</td>
<td>264</td>
<td>8.2</td>
<td>873</td>
<td>5.0</td>
<td>2.21</td>
<td>9.3</td>
</tr>
<tr>
<td>17:6:8:71 rice, mung beans, groundnuts, water</td>
<td>751</td>
<td>40</td>
<td>7</td>
<td>136</td>
<td>0.72</td>
<td>0.27</td>
<td>77</td>
<td>6.4</td>
<td>772</td>
<td>4.4</td>
<td>1.34</td>
<td>10.6</td>
</tr>
<tr>
<td>17:6:8:71 rice, mung beans, sesame, water</td>
<td>846</td>
<td>29</td>
<td>28</td>
<td>119</td>
<td>0.90</td>
<td>0.26</td>
<td>342</td>
<td>9.9</td>
<td>891</td>
<td>5.5</td>
<td>1.63</td>
<td>11.1</td>
</tr>
<tr>
<td>20:3:8:71 rice, dried fish, groundnuts, water</td>
<td>783</td>
<td>42</td>
<td>11</td>
<td>133</td>
<td>0.64</td>
<td>0.21</td>
<td>364</td>
<td>6.2</td>
<td>1049</td>
<td>9.2</td>
<td>1.35</td>
<td>6.6</td>
</tr>
<tr>
<td>20:3:6:71 rice, dried fish, sesame, water</td>
<td>878</td>
<td>31</td>
<td>32</td>
<td>116</td>
<td>0.82</td>
<td>0.20</td>
<td>628</td>
<td>9.8</td>
<td>1168</td>
<td>10.4</td>
<td>1.65</td>
<td>7.2</td>
</tr>
</tbody>
</table>

continues
<table>
<thead>
<tr>
<th>Complementary foods based on starchy roots, tubers, and similar foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:18:24:45 banana flour, peanuts, sugar, water</td>
</tr>
<tr>
<td>72:12:4:8:4 coco yam, avocado, soya beans, coconut milk, pumpkin leaf</td>
</tr>
<tr>
<td>63:17:8:2:10 potato, kale, chick-pea flour, oil, water</td>
</tr>
<tr>
<td>47:28:6:3:3:13 sweet potato, egg, dried skim milk, oil, brown sugar, water</td>
</tr>
<tr>
<td>35:12:41:12 sweet potato, pumpkin leaves, water, mackerel</td>
</tr>
<tr>
<td>16:1:10:4:69 sago flour, wheat, brown sugar, oil, water</td>
</tr>
<tr>
<td>Estimated need from complementary food for 9- to 11-mo-old infant (see text)</td>
</tr>
</tbody>
</table>

For origin of recipes, see ref. 28. Estimated need from complementary food for iron (10.8 mg/d) is based on the basal requirement estimate and intermediate (i.e., 10%) bioavailability (3). When bioavailability is low (i.e., 5%), estimated need is 20.8 mg Fe/d; when high (i.e., 15%), estimated need is 6.8 mg Fe/d. Estimated need from complementary food for zinc (2.66 mg/d) is based on basal requirement estimate and moderate bioavailability (i.e., 35%). When bioavailability is low (i.e., 5%), estimated need is 7.26 mg Zn/d; when high (i.e., 55%), estimated need is = 1.46 mg Zn/d (3) CHO, carbohydrate; DF, dietary fiber as nonstarch polysaccharide; Phy, phytic acid.

Adapted from Gibson RS et al. (28).
<table>
<thead>
<tr>
<th>TABLE 4. Calculated energy and nutrient content (per 100 kcal as eaten) of selected complementary foods</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td><strong>Maize and wheat-based complementary foods</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td>17:10:5:68 unrefined maize flour, cow peas, groundnuts, water</td>
</tr>
<tr>
<td>8:2:90 unrefined maize flour, soya flour, water</td>
</tr>
<tr>
<td>22:6:7:2 unrefined maize flour, soya flour, water</td>
</tr>
<tr>
<td>20:3:4:1:72 unrefined maize flour, soya flour, groundnuts, water</td>
</tr>
<tr>
<td>20:6:7:2 refined maize flour, soya flour, groundnuts, sorghum,</td>
</tr>
<tr>
<td></td>
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<tr>
<td><strong>Rice-based complementary foods</strong></td>
</tr>
<tr>
<td></td>
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<tr>
<td>4:1:7:1:87 rice, kidney beans, roasted sesame, sugar, water</td>
</tr>
<tr>
<td>30:7:4:59 rice, mung beans, ghee, water</td>
</tr>
<tr>
<td>18:3:12:4:63 rice, sorghum, brown sugar, oil, water</td>
</tr>
<tr>
<td>28:3:1:68 rice, groundnut flour, sugar, water</td>
</tr>
<tr>
<td>20:4:4:72 rice, soya flour, groundnuts, water</td>
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<tr>
<td>20:4:4:72 rice, soya flour, sesame, water</td>
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<tr>
<td>17:6:6:71 rice, mung beans, groundnuts, water</td>
</tr>
<tr>
<td>17:6:6:71 rice, mung beans, sesame, water</td>
</tr>
<tr>
<td>20:3:6:71 rice, dried fish, groundnuts, water</td>
</tr>
<tr>
<td>20:3:6:71 rice, dried fish, sesame, water</td>
</tr>
<tr>
<td></td>
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<tr>
<td><em>continues</em></td>
</tr>
<tr>
<td>Complementary foods based on starchy roots, tubers, and similar foods</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>13:18:24:45 banana flour, peanuts, sugar, water</td>
</tr>
<tr>
<td>72:12:4:8:4 coco yam, avocado, soya beans, coconut milk, pumpkin leaf</td>
</tr>
<tr>
<td>63:17:8:2:10 potato, kale, chick-pea flour, oil, water</td>
</tr>
<tr>
<td>47:28:6:3:13 sweet potato, egg, dried skim milk, oil, brown sugar, water</td>
</tr>
<tr>
<td>35:12:41:12 sweet potato, pumpkin leaves, water, mackerel</td>
</tr>
<tr>
<td>16:1:10:4:69 sago flour, wheat, brown sugar, oil, water</td>
</tr>
<tr>
<td>Desired nutrient density (see text)</td>
</tr>
</tbody>
</table>

For origin of recipes, see ref. 28. Desired nutrient density for iron based on low bioavailability is 4.6 mg/100 kcal, for intermediate 2.4 mg/100 kcal, and for high 1.5 mg/100 kcal. Desired nutrient density for zinc based on low bioavailability is 1.6 mg/100 kcal, for moderate 0.6 mg/100 kcal, and for high 0.3 mg/100 kcal (3). CHO, carbohydrate; DF, dietary fiber as nonstarch polysaccharide; Phy, phytic acid. Adapted from Gibson RS et al. (28).
However, to assess whether a deficiency of any of these "at-risk" micronutrients has an influence on linear growth during complementary feeding requires a review of observational (34) and well-designed double-blind clinical trials; these are summarized below. Only the results of clinical trials can be used to confirm a causal role for a specific nutrient deficiency in linear growth retardation.

Some of the at-risk nutrients in complementary diets have a direct effect on linear growth (e.g., protein, zinc, calcium, phosphorus, vitamin A, and iodine); these are discussed individually. Others such as iron, riboflavin, zinc, and vitamin A influence growth indirectly through their effects on appetite, immune competence, and intestinal structure and function.

Growth-Limiting Nutrients with a Direct Role in Linear Growth

Linear growth is a function of the growth and development of the long bones, the formation of a collagenous matrix within which the deposition of bone mineral crystals can take place. In linear growth retardation, the length of the long bones is retarded by diminished growth of epiphyseal cartilage. The latter becomes narrow, with a decreased rate of chondrocyte proliferation. In particular, the synthesis of bone matrix collagen is said to be depressed (35). Whether bone mineralization and resorption of bone mineral are affected in linear growth retardation in children is controversial and probably depends on the nutrient deficit.

Nutrients shown to be inadequate in complementary diets and with a direct effect on linear growth include calcium and zinc and, in some circumstances, protein, phosphorus, iodine, and vitamin A. The mechanism whereby each of these nutrients influences linear growth, together with the available evidence for its role as growth determinant, is discussed briefly in turn below.

Protein

Proteins are required in the complementary diet both as a source of essential amino acids for protein synthesis and as a source of nitrogen for the synthesis of nonessential amino acids and other nitrogen-containing compounds.

Results of early studies led to the view that protein deficiency and energy deficiency were major causes of linear growth failure in early childhood (36,37). However, because of their design, it was not possible to distinguish between the effects of protein *per se* in these early studies and those of other growth-limiting nutrients (e.g., calcium, zinc, or phosphorus) that were added simultaneously to the diet.

Recent evidence suggests that the amount of protein consumed by exclusively breast-fed infants between 4 and 6 months of age is adequate and unlikely to limit their growth at that time (38). However, from 6 months of age, most breast-fed infants require some additional protein from complementary foods to meet their estimated needs (3). The levels required are small, ranging from 2 g/day for 6- to 8-month-old infants receiving an average intake of breast milk to 9.1 g/day for infants aged 12–23 months who are receiving a low intake of breast milk (3). Comparison of
both actual (Table 2) and theoretical (Table 3) intakes with these estimated needs suggests that most complementary foods used in developing countries provide sufficient protein, even after digestibility and amino acid score are taken into account. Hence, deficits in protein are unlikely to be a primary factor limiting growth, even in infants receiving only plant-based complementary foods, with the possible exception of those based on sago or cassava (Table 3) (28).

Beaton et al. (39) reached a similar conclusion after examining the adequacy of protein intakes for toddlers (aged 18–30 months) from selected communities in Egypt, Kenya, and Mexico in the Nutrition Collaborative Research Support Program (CRSP) study. They also emphasized that even when breast-feeding ceased, the toddler’s existing protein intakes were unlikely to be a primary factor limiting their growth. Moreover, only a marginal benefit would be achieved by increasing the content of lysine, the amino acid found to be most limiting in the diets of the Kenyan children.

**Zinc**

Growth failure is a prominent feature of zinc deficiency: Physical, skeletal, and muscle growth are affected. The magnitude of the growth failure and its response to zinc supplementation depend on the severity of the zinc deficiency state and the extent to which zinc is the first growth-limiting nutrient. In chronic mild zinc deficiency, growth retardation often occurs before tissue zinc concentrations or total body zinc content is significantly reduced (40).

The mechanisms underlying the retarded growth that occurs in zinc deficiency are not well established. The role of zinc in protein synthesis and gene expression, and thus in the essential processes of cell differentiation and replication, is likely to be crucial. Hormonal imbalances, specifically those mediated through changes in the production or secretion of growth hormone and insulin-like growth factor-1, may also play a role (41).

To date, there is little evidence that exclusively breast-fed full-term infants are susceptible to zinc deficiency before 6 months of age (10,22,42,43), despite the dramatic decline in breast milk zinc concentrations that occurs during the first 3 months of lactation (44). That they are not is in part because of the high bioavailability of zinc in breast milk, combined with an efficient mechanism for conserving intestinal endogenous zinc (45).

Nevertheless, some (46–56), but not all (57–64), randomized double-blind placebo-controlled trials in both industrialized and developing countries have reported modest but statistically significant improvements in linear growth and, in some cases, body weight following supplementation with physiological levels of zinc. Some of these studies were carried out on severely malnourished infants and children with a propensity for catchup growth (50,57,62). Only a few have been conducted on apparently healthy infants during the complementary feeding period (46,49,53,54,56,58), most of which reported a positive impact of zinc on linear growth, suggesting that zinc was the primary growth-limiting nutrient. A low zinc content in breast milk was unlikely to be responsible for this deficit because the
concentration of zinc in breast milk is typically unaffected by maternal diet (27). Instead, the suboptimal zinc status was probably induced by the high requirements of zinc for growth at this time coupled with some displacement of breast milk by complementary foods with a low content and bioavailability of zinc. However, in most of the studies, no details of the timing and composition of the complementary foods were given.

The bioavailability of zinc in complementary foods based on cereals and legumes is likely to be poor because they contain a relatively high content of phytic acid (Table 5), which forms insoluble complexes with zinc (and iron and calcium), inhibiting zinc absorption (65). The negative effect of such complexes on zinc absorption can be predicted by phytate/zinc molar ratios when the dietary zinc intake is close to the requirement (66). Ratios above 15 are known to compromise zinc status (23). Note that the phytate/zinc ratios of the cereal-based complementary foods shown in Table 5 are all above 15; hence, it can be assumed that there is low zinc bioavailability (around 15%) (23). By contrast, the phytate/zinc ratios of complementary foods based on starchy roots and tubers are much lower, generally below 15, but they also usually have a much lower zinc content than those based on cereals and legumes. High levels of calcium are known to exacerbate the inhibitory effect of phytate on zinc absorption (67). However, the calcium content of most plant-based complementary foods is too low to have any detrimental effect, unless they are prepared from lime-soaked maize.

Such differences in the bioavailability of zinc in complementary foods have a marked impact on the estimated needs for zinc in infants of various ages. Hence, if infants receive complementary foods containing a high content of phytic acid and thus have poor zinc availability, they are likely to be at high risk of zinc deficiency. Furthermore, high-phytate complementary foods, when consumed with breast milk, may actually compromise the bioavailability of zinc (and iron) from breast milk. Bell et al. (15), using an in vivo absorption rat pup model, showed that even commercially processed infant cereals lowered $^{65}$Zn uptake from extrinsically radiolabeled milk diets.

As noted above, not all the zinc supplementation trials in apparently healthy infants (58) and children (59–61,63,64) have shown a positive linear growth response. Such discrepancies in the responses observed may be associated with the age and gender of the children studied, the co-existence of other growth-limiting micronutrient deficiencies, inadequate sample size and study design, and the dose, frequency, type, compliance, and duration of the zinc supplement used. In addition, differences in the initial zinc or growth status of the infants and children may have influenced the responses observed (53,58). Certainly, Brown et al. (68), in their meta-analysis of 22 double-blind zinc supplementation studies of children younger than 13 years from both industrialized and developing countries, reported that a highly significant positive effect of zinc supplementation on change in height was present only for those children with mean initial height-for-age $z$ scores of less than or equal to −2.0 but not for those with mean initial height-for-age $z$ scores of greater than or equal to −2.0. Changes in height and weight were also negatively associated with mean initial
<table>
<thead>
<tr>
<th>TABLE 5. Calculated energy and selected nutrient and antinutrient content (per 100 g as eaten) of some complementary foods</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Maize and wheat-based complementary foods</td>
</tr>
<tr>
<td>17:10:5:68 unrefined maize flour, cow peas, groundnuts, water</td>
</tr>
<tr>
<td>8:2:90 unrefined maize flour, soya flour, water</td>
</tr>
<tr>
<td>22:6:72 unrefined maize flour, soya flour, water</td>
</tr>
<tr>
<td>20:3:4:1:72 unrefined maize flour, soya flour, groundnuts, sorghum, water</td>
</tr>
<tr>
<td>20:6:2:72 unrefined maize flour, groundnuts, sorghum, water</td>
</tr>
<tr>
<td>22:6:72 refined maize flour, soya flour, water</td>
</tr>
<tr>
<td>15:12:3:2:68 wheat, brown sugar, oil, sorghum, water</td>
</tr>
<tr>
<td>Rice-based complementary foods</td>
</tr>
<tr>
<td>4:1:7:1:87 rice, kidney beans, roasted sesame, sugar, water</td>
</tr>
<tr>
<td>30:7:4:59 rice, mung beans, ghee, water</td>
</tr>
<tr>
<td>18:3:12:4:63 rice, sorghum, brown sugar, oil, water</td>
</tr>
<tr>
<td></td>
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<tr>
<td>Energy (kcal)</td>
</tr>
<tr>
<td>116</td>
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<tr>
<td>38</td>
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<td>106</td>
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<td>105</td>
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<td>161</td>
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<td>115</td>
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<tr>
<td>Nutrient Information</td>
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</tr>
<tr>
<td>28:3:1:68 rice, groundnut flour, sugar, water</td>
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<tr>
<td>20:4:4:72 rice, soya flour, groundnuts, water</td>
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<tr>
<td>20:4:4:72 rice, soya flour, sesame, water</td>
</tr>
<tr>
<td>17:6:6:71 rice, mung beans, groundnuts, water</td>
</tr>
<tr>
<td>17:6:6:71 rice, mung beans, sesame, water</td>
</tr>
<tr>
<td>20:3:6:71 rice, dried fish, groundnuts, water</td>
</tr>
<tr>
<td>20:3:6:71 rice, dried fish, sesame, water</td>
</tr>
</tbody>
</table>

**Complementary foods based on starchy roots, tubers, and similar foods**

<table>
<thead>
<tr>
<th>Nutrient Information</th>
<th>Quantity</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:18:24:45 banana flour, peanuts, sugar, water</td>
<td>206</td>
<td>8.1</td>
</tr>
<tr>
<td>72:12:4:8:4 coco yam, avocado, soya beans, coconut milk, pumpkin leaf flour, oil, water</td>
<td>114</td>
<td>2.8</td>
</tr>
<tr>
<td>63:17:8:2:10 potato, kale, chick-pea flour, oil, water</td>
<td>123</td>
<td>2.8</td>
</tr>
<tr>
<td>47:28:6:3:3:13 sweet potato, egg, dried skim milk, oil, sugar, water</td>
<td>160</td>
<td>6.3</td>
</tr>
<tr>
<td>35:12:41:12 sweet potato, pumpkin leaves, water, mackerel sugar, oil, water</td>
<td>74</td>
<td>3.3</td>
</tr>
<tr>
<td>16:1:10:4:69 sago flour, wheat, brown sugar, oil, water</td>
<td>133</td>
<td>0.2</td>
</tr>
</tbody>
</table>

For origin of recipes, see ref. 28. CHO, carbohydrate; DF, dietary fiber as nonstarch polysaccharide; Phy, phytic acid; [Phy]/[Zn], Phytate/Zinc molar ratio.
plasma zinc. Finally, in some of the studies, other factors modulating the growth response may have been concurrent infection, long-term effects of prenatal malnutrition, and intergenerational effects of maternal malnutrition.

In general, zinc deficiency appears to have a greater impact on linear growth in male than female subjects (46,49,52,53,55). The reason for this has not yet been clearly established. The males of most species, including humans, have a higher percentage of total body weight composed of muscle, which in turn contains a higher content of zinc than does fat. Additionally, the growth rate of males is generally greater than that of females, so their zinc requirements are probably greater.

**Calcium and Phosphorus**

Calcium and phosphorus are the most abundant minerals in the body. More than 99% of calcium and 80% of phosphorus in the body are stored in bone, mainly as the salt hydroxyapatite \([\text{Ca}_{10}(\text{OH})_2(\text{PO}_4)_6]\), which gives rigidity to the skeleton. Young bone generally contains calcium and phosphorus in the proportion 1.7:1 to 2.14:1 g/g, increasing to 2.3:1 g/g in adult human bone. During periods of rapid growth such as early infancy, calcium and phosphorus accretion rates for skeletal growth are very high. For infants between 0 and 4 months, estimated accretion rates are 155 mg/day of calcium and 79 mg/day of phosphorus, decreasing slightly between 4 and 12 months to 130 mg/day for calcium and 66 mg/day for phosphorus (69).

The low calcium content of most plant-based complementary foods used in developing countries results in calcium intakes and densities below the theoretical estimated needs for infants and toddlers in all three age groups (Tables 2–4). These calcium deficits increase even further as breast-feeding ceases, at which time calcium intakes become very close to the biological requirements for many children in developing countries. A notable exception is found in Mexican infants and toddlers, whose calcium intakes are derived from corn soaked in lime. In the CRSP study, for example, 90% of the non-breast-feeding toddlers in Egypt and 88% in Kenya, compared with only 2% in Mexico, were estimated to have inadequate calcium intakes (70). The bioavailability of calcium from many plant-based complementary foods is likely to be much lower than that from breast milk, owing to the presence of phytates and oxalates in cereals and uronic acid in the fiber of fruits and vegetables. Hence, theoretically, by about 1 year of age, skeletal growth could be limited by an inadequate supply of calcium.

Nevertheless, there are very few reports of linear growth failure, abnormal bone formation, rickets, or biochemical signs of hyperparathyroidism associated with low calcium intakes in infants and children in developing countries. However, only one small calcium supplementation study on 38 Indian infants aged 6–30 months has been carried out in the complementary feeding period (71). Infants were given either 2.5 or 3 g of calcium glycerophosphate (191 mg of Ca/g; 140 mg of P/g) six times a week for 42 weeks, the dose depending on whether they were younger or older than 1 year. After 42 weeks, no significant differences in length or weight gain, radiographic bone dimensions, or appearance of ossification centers were observed among the two groups.
There are several reports of calcium supplementation studies in older children in developing countries. Most but not all (72–74) have been reviewed in detail by Prentice and Bates (69). Of these, only two reported significant but modest improvements in growth velocity (both height and weight) in calcium-supplemented children (75,76), which may have been caused by an increase in appetite due to the calcium salt, as speculated by Walker (77). Nevertheless, there has been some evidence of inadequate calcium intakes in South African children, with biochemical signs of hyperparathyroidism (low serum calcium and raised serum alkaline phosphatase), which normalized after calcium supplementation (mainly, calcium lactate/gluconate) (78). Reductions in forearm bone mineral content in relation to body size have also been reported in some Gambian children with low calcium intakes (76,79).

Most plant-based complementary foods are likely to have a high phosphorus content, with the notable exception of those prepared from “sticky rice.” Indeed, in the CRSP study of children consuming maize-based (Mexico and Kenya) and wheat-based (Egypt) diets, phosphorus intakes were considerably higher than calcium intakes, and very few of the children had intakes of phosphorus low enough to be inadequate (70). Nonetheless, a possible role of phosphorus deficiency in stunting was suggested by Fraser (35). Indeed, in a study of Thai children, phosphorus deficiency—based on low serum and urinary phosphorus (and calcium) levels—was described in short children, attributed to the consumption of sticky rice. No other differences existed for serum levels of calcium, alkaline phosphatase, and vitamin D between the tall and stunted children (80).

Low calcium intakes have been said to increase the requirements for vitamin D (81). This hypothesis may explain in part the high prevalence of rickets in certain regions (e.g., North Africa, Egypt, Iran, North India, and China) where dietary calcium intakes are low and poorly available and skin synthesis of vitamin D is limited because infants and children are covered to prevent exposure to the sun (82).

In summary, despite the suggestion that calcium intakes probably become limiting after the first 6 months when infants are no longer fully breast-fed and are receiving plant-based complementary foods, severe nutritional deficiency of calcium is rare, possibly because of adaptive mechanisms such as increased absorption and decreased losses. Marginal calcium deficiency based on low serum calcium and raised alkaline phosphatase levels as well as low bone mineral content have been described, but the evidence that calcium deficiency per se is a cause of linear growth faltering is inconclusive. As an inadequate supply of several nutrients is likely in complementary diets, calcium is rarely likely to be the first growth-limiting nutrient. More studies are required to elucidate whether nutritional phosphorus deficiency may be a factor limiting linear growth of infants fed sticky rice.

Iodine

Iodine is necessary for the normal production of thyroid hormones: thyroxine (3,5,3',5'-tetraiodothyronine; T4), containing four atoms of iodine, and T3 (3,5,3'-triiodothyronine), containing three. These hormones are necessary for normal
physical growth, nervous system development, temperature regulation, nerve conduction, and a variety of other important functions.

There is no evidence that iodine per se has any role in growth, except through the mediation of thyroid hormones. Thyroxine and T3 influence growth through their role in the secretion of growth hormone by the pituitary gland as well as the cellular response to insulin-like growth factor-1. T3 influences the development of the epi- physeal cartilage, its calcification, and the proliferation of blood vessels (83). When the synthesis of thyroid hormones is compromised by a low iodine supply, both postnatal linear growth and bone maturation are retarded.

Iodine deficiency occurs in many areas of the world where the soil is low in iodine. Its effects are accentuated by the consumption of certain foods that contain goitrogenic substances, such as cassava, millet, sweet potato, and various beans, all foods that are often used during complementary feeding in developing countries. In areas where iodine deficiency and endemic goiter are severe, endemic cretinism sometimes occurs, resulting in severe retardation of linear growth and bone maturation, which can be partly reversed by iodine supplementation (84).

In geographic areas where the iodine supply of pregnant and lactating mothers is low, their breast milk iodine content may be compromised. Neonates have low iodine stores at birth (85), so if they receive breast milk with a low iodine content, they may be at risk of iodine deficiency, which may persist if the plant-based complementary foods are grown in iodine-deficient soils and are goitrogenic. Even breast-fed infants of iodine-replete mothers who are living in a non-iodine-deficient area may have a low iodine status; breast milk and cereal-based porridges are relatively poor in iodine (86).

There is some evidence that even moderate iodine deficiency may impair linear growth. In the nutrition CRSP study, for example, low thyroid hormones (T3, T4, free T4) were reported in 11% of Kenyan schoolchildren and raised thyroid-stimulating hormone in 10%. Furthermore, in Kenyan schoolchildren, serum free T4 levels and iodized salt in the households were each positively associated with toddlers’ height (p = 0.04), even after controlling for socioeconomic status (34).

Vitamin A

Vitamin A is required for sustained growth even in the absence of infection, although the specific mechanisms involved are still poorly understood. It appears to have a direct metabolic effect on bone growth by modulating the growth of bones through remodeling. Vitamin A is necessary for the activity of cells in the epiphyseal cartilage, which must undergo a normal cycle of growth, maturation, and degeneration to permit normal bone growth. In addition, retinoic acid, an active metabolite of vitamin A, activates gene transcription by way of a nuclear receptor and may also have a role in growth hormone-induced growth through its link with thyroid hormone (87).

Breast-feeding normally protects against vitamin A deficiency in infancy. However, breast-fed infants of mothers with marginal vitamin A status as well as preterm and small-for-gestational-age infants with low vitamin A stores may have suboptimal biochemical vitamin A status, and this may persist if they are fed
complementary foods with low vitamin A activity. Unfortunately, in many developing countries, vitamin A-rich foods are underutilized in the diets of weaning-age children, often because green leafy vegetables, although often available, are considered too bland, bitter, unhealthy, or fibrous for infants and young children (88). In some cases, mothers also lack knowledge on how to prepare green leafy vegetables for complementary feeding. In the Nutrition CRSP study, 68% of Mexican toddlers were predicted to have inadequate intakes of vitamin A compared with 32% of Egyptian toddlers (89).

Whether vitamin A deficiency per se has a major impact on linear growth during the complementary feeding period is difficult to establish. Several cross-sectional studies have reported an association between suboptimal vitamin A deficiency and stunting (90,91). However, in most of these studies, severe infection or the co-existence of other nutrient deficiencies makes it impossible to attribute a specific growth-depressing role to vitamin A deficiency alone in these children (92). Even in double-blind vitamin A supplementation trials, no consistent linear growth effects during infancy or childhood have been reported. In three large community-based trials in Indonesia, two of which involved the administration of vitamin A capsules at 6 monthly (93) or 4 monthly (94) intervals and the third using vitamin A-fortified monosodium glutamate (95), modest improvements in linear growth were reported in only two of the trials (94,95) and there was no improvement in weight gain. In the most recent Indonesian trial (94), both linear and ponderal growth improved significantly in those infants with very low initial serum retinol values (i.e., <0.35 μmol/L), an effect that was modified by age and breast-feeding.

Some of these discordant findings may thus reflect in part differences in initial vitamin A status, age, and breast-feeding status as well as length of the study period, dose and mode of delivery of vitamin A, and, most importantly, the existence of other potentially confounding factors such as concurrent multiple micronutrient deficiencies and infections. A linear growth response to vitamin A can be expected only when vitamin A is the first limiting nutrient.

Growth-Limiting Nutrients with an Indirect Role in Linear Growth

Nutrient deficiencies occurring during the complementary feeding period may have a secondary impact on growth, induced by impairment of appetite, intestinal structure or function, or immune competence. For example, in iron and zinc deficiency, anorexia is common; in zinc, riboflavin, and vitamin A deficiency, intestinal structure and function are compromised; whereas in iron, zinc, and vitamin A deficiency, immune competence is reduced. Furthermore, interactions occur among deficiencies of micronutrients (e.g., zinc and vitamin A, vitamin A and iodine), some of which may exacerbate linear growth retardation during the complementary feeding period.

Iron

There is ample evidence that iron deficiency anemia is widespread in infants in both industrialized and developing countries (96), especially after 4–6 months of age,
when the infant’s iron stores are usually depleted. The relation between iron deficiency anemia and linear growth faltering during infancy is less convincing than for zinc deficiency. This is probably because unlike zinc, iron does not have such a direct biological role in growth. Instead, its effect on growth is secondary, mediated by the anorexia or increased morbidity that often occurs as a result of iron deficiency anemia. In addition, the action of iron on oxidative processes may stimulate the growth rate.

To our knowledge, the only two iron supplementation studies carried out in early childhood—when complementary feeding may have been given—measured changes in ponderal but not linear growth (97,98). They both reported significant weight gains in anemic infants given iron supplements, but only one of these studies was a double-blind design (98). In the latter, British infants aged 17–19 months were given 24 mg of iron/day in combination with vitamin C for 8 weeks; those with the greatest hematological response to iron showed the fastest weight gain. The authors speculated that the enhanced weight gain might be attributable to a correction of anorexia, although no data were provided to support their hypothesis.

Several iron supplementation trials in older children have assessed changes in both linear and ponderal growth (61,99–104). Of these, three reported a positive effect of iron supplements on linear growth (101,103,104) but only in the anemic children; two of these also observed an improvement in weight gain (101,103). In the Indonesian studies, the improved growth was attributed to a significant reduction in morbidity (101,104), whereas in the Kenyan study, an improvement in appetite was implicated (103). Reduced morbidity is likely to enhance the utilization of nutrients, resulting in a greater production of cellular energy and accelerated protein anabolism.

In most of these studies, iron supplementation was given for relatively short periods, ranging from 8 to 22 weeks, which could have been too short in some cases to detect any differences in linear growth, although even supplementation with iron for 1 year did not enhance weight or length gain of anemic, iron-deficient Mexican children (61). Alternatively, the level of iron supplement given may have been too low (99), or iron was not the first limiting nutrient. Complementary diets that induce iron deficiency are also likely to have a low content and bioavailability of zinc.

Zinc

Zinc may also influence linear growth indirectly through its role in neurosensory and immune function as well as through its interaction with vitamin A. In zinc deficiency, the rate of production of retinol-binding protein is decreased and possibly the absorption of vitamin A (105). Decreased taste acuity (hypoguesia) has been described in mild zinc deficiency in some infants (106) and children (51,107). Its role in appetite is complex, but it is assumed to contribute to the anorexia seen in zinc deficiency (108) and thus to have an indirect effect on growth.

Immune competence is also reduced in zinc deficiency, so resistance to infection is decreased. Indeed, several randomized placebo-controlled zinc supplementation trials in developing countries have reported improved immune function or reductions
in the incidence of diarrhea, respiratory infections, or malaria (109), some of which have been conducted in infants during the complementary feeding period (50,54,56–58,60,62,110–114). Furthermore, zinc supplementation of infants with acute and persistent diarrhea has been shown to improve mucosal integrity (115). In some of these infant studies, concomitant improvements in linear growth and immune function have also been observed in the zinc-supplemented group (50,54,56), as discussed above.

Riboflavin

Riboflavin deficiency affects growth indirectly, in part because of inefficient use of dietary energy. This is attributed to the role of flavins in the oxidative steps of metabolism as well as to disturbances in gastrointestinal morphology and cytokinetics. Regarding the latter, one of the earliest defects is a failure to produce the normal number of villi in the duodenum, an effect known to interfere with absorption of nutrients, especially iron (116,117).

Most infants appear to receive the necessary amount of riboflavin from complementary foods to meet their estimated needs (Tables 1–3), unless foods based almost exclusively on rice, millet, sorghum, and sago are used. However, in some countries (e.g., rural Gambia), mothers may be severely riboflavin deficient. In such cases, breast milk riboflavin levels are often very low (27), and low biochemical riboflavin status is not uncommon among breast-fed infants and weanlings in the Gambia (118). Once breast-feeding ceases, the risk of riboflavin deficiency during early childhood increases in many developing countries because intakes of meat, fish, and dairy products are often low. For example, in the Nutrition CRSP study, risk of inadequate intakes of riboflavin was 20% and 52% for Egyptian and Mexican toddlers, respectively (89). Indeed, angular stomatitis and biochemical ariboflavinosis have been reported in rural preschoolchildren in Northeast Thailand, consuming predominantly rice-based diets (119). Nevertheless, the biochemical response to varying intakes of riboflavin is not consistent, suggesting that differing requirements probably exist, depending on factors such as infection and possibly other concurrent nutrient deficiencies (120). To our knowledge, no trials have examined the impact of a riboflavin supplement alone on linear growth during the complementary feeding period.

Vitamin A

Vitamin A deficiency may also have an indirect effect on linear growth through its influence on infectious morbidity such as diarrheal episodes. In circumstances where zinc, vitamin A, and iodine deficiencies co-exist, diarrheal episodes may be exacerbated because of the interactions between vitamin A and zinc or vitamin A and iodine deficiency (105).

Deficiency of vitamin A is associated with impaired humoral and cellular immunity and with decreased activity of complement in serum and of lysozyme in leukocytes. Deficiency also has marked effects on the integrity of mucous membranes.
They become keratinized, with a reduced production of secretory IgA and mucus, changes that reduce their resistance to penetration by bacteria (121). Hence, it is not surprising that vitamin A deficiency is associated with increased susceptibility to respiratory and gastrointestinal disease, which in turn may lead to linear growth retardation. Very few of the controlled trials of vitamin A supplementation and morbidity, however, have evaluated the effects on linear and ponderal growth as well as morbidity (121). An exception was the controlled trial of Rahmatullah et al. (122) on Indian children aged 6–60 months. However, no improvement in either morbidity or linear growth was reported in those children receiving a weekly low-dose vitamin A supplement for 12 months compared with the control subjects.

Summary

In summary, the studies reviewed above—designed to correct a deficiency of individual growth-limiting nutrients by supplementation—have produced inconsistent results on linear growth, with the exception of those on zinc during the complementary feeding period. Several methodological reasons have been put forward for these discrepancies; these have been discussed for each nutrient in turn. However, one of the main reasons for the inconsistencies is the probable co-existence of multiple nutrient deficiencies. This is discussed in more detail below.

QUANTITY AND DIETARY QUALITY OF COMPLEMENTARY FOODS AND THEIR ROLE IN LINEAR GROWTH

Both the quantity and the quality of complementary foods contribute to the adequate intake of growth-limiting nutrients from the complementary diet. Several factors can limit the quantity of food consumed daily by young children and have been reviewed in detail by Brown (123) and WHO (3). In brief, these include infrequent feeding, lack of encouragement from the caregiver, anorexia caused by illness or specific micronutrient deficiencies, poor intake because of unfavorable organoleptic quality of foods [including high viscosity (124)], and limited food resources.

The amount of food consumed per meal by infants is limited by their gastric capacity. Consequently, if foods contain low levels of nutrients, the amount of food required to meet nutrient needs may exceed the gastric capacity of the child within a given number of feeds per day. Infants can self-regulate the volume of breast milk or breast milk substitute consumed, depending on energy density (125,126). That is, with the high energy density of breast milk or substitutes, lower volumes will be consumed. Also, when the intake of complementary foods is increased, the energy intake from breast milk is reduced (127). Displacement of breast milk by complementary foods with a low nutrient density (a low amount of nutrient/kcal; e.g., high-fat foods, nonnutritive carbohydrates) may provide sufficient energy to meet estimated energy needs, but daily intakes of growth-limiting nutrients will be compromised.

Some studies have attempted to assess the impact of quantity versus dietary quality on linear growth. For example, a study of New Guinean boarding school children
by Malcolm (36) showed that linear growth was improved by 40% when the intake of usual foods was increased compared with 111% when the usual diet was supplemented with skimmed milk powder, a high-quality food. By contrast, a margarine supplement, which increased energy intake only, had no effect on linear growth. No comparable studies have been conducted in breast-fed infants. Instead, regression analysis has been used to compare the expected impact of increased feeding frequency or increased energy density of the complementary diet on the total energy intake from complementary foods in different geographic settings (3). This approach could be used in future studies to compare the predicted efficiency of increasing either the quantity or the quality of the diet for improving intakes of growth-limiting nutrients among breast-fed children.

Improving Dietary Quality with Multiple Micronutrient Supplements

Inadequacies of multiple nutrients are likely to occur during complementary feeding in developing countries, as discussed above. A recent study of infants in rural Malawi showed that intakes of energy, calcium, iron, zinc, vitamin A, and riboflavin from complementary foods were below estimated needs (C. Hotz and R. S. Gibson, unpublished data), as were intakes of energy, calcium, iron, and zinc from complementary foods among Zambian children (26). In addition, dietary and biochemical data of toddlers in Mexico, Kenya, and Egypt indicated that more children were at risk of at least two micronutrient deficiencies than just one (34,61,128).

In view of these findings, supplementing infants during the complementary feeding period with a single nutrient, as discussed above, is unlikely to enhance linear growth, unless that specific nutrient is the first limiting nutrient. Hence, in the experimental studies already reviewed, failure to obtain a positive effect on linear growth in the nutrient-supplemented group does not necessarily indicate the absence of that nutrient deficiency in the study population. In this section, we review the available studies designed to assess the impact of multiple micronutrient supplements on linear growth. Very few supplementation trials, however, have examined the effect of two or more micronutrients on linear growth during the complementary feeding period. Furthermore, very few have been designed to identify which specific growth-limiting micronutrients may be responsible for any changes in linear growth observed.

One of the earliest studies to examine the effect on linear growth of a multiple micronutrient supplement (thiamin, riboflavin, folic acid, niacin, vitamin B₆, folic acid, vitamin B₁₂, vitamin A, calcium, iron, zinc, and iodine), with and without a high-energy biscuit, was carried out in northern Thailand in a daycare setting. The investigators combined a study of growth of preschool children aged from under 1 to 5 years with a sanitation-health intervention (129). No differences in length and weight were noted over the 22-month study among the intervention groups overall or among the preschool children with the greatest height and weight deficits at the beginning of the study. This finding was not explicable on the basis of morbidity, seasonal differences in growth rates, poor compliance, or, according to the investigators, dietary intakes, although no detailed data on home food intakes or breast milk intakes were collected.
In addition, the number of infants younger than 12 months, when impaired linear growth is most likely to occur, was small.

A more recent study on Mexican preschoolchildren aged 18–36 months also found no improvement in linear growth in children receiving separate and combined iron and zinc supplements 5 days per week for 12 months, despite marked increases in plasma and red blood cell zinc and plasma ferritin in the iron-supplemented groups (61). A large proportion of these same children also had a low tocopherol (64%), retinol (24%), and vitamin B₁₂ (33%) biochemical status as well as low biochemical indexes of iron and zinc, which could have been limiting growth. In view of the existence of these multiple micronutrient deficiencies in these Mexican children, a second double-blind intervention study was undertaken in which children aged 8–14 months received, under supervision, a flavored beverage containing 30 kcal and multiple micronutrients \( n = 168 \) or the 30-kcal flavored beverage with no micronutrients added \( n = 167 \) for 6 days a week over 12 months. In contrast to the earlier Mexican study (61), a significant increase in final length (but not weight) was observed in the multiple micronutrient-supplemented group compared with the placebo, most notably among those children of low and median socioeconomic status, who grew approximately 1 cm more than their placebo counterparts (128). Furthermore, the effect of the micronutrient supplement on linear growth was larger in the infants aged under 12 months at baseline. Nevertheless, the actual increase in linear growth was still less than the potential increment expected, perhaps because of the constraints on growth arising from prenatal malnutrition or intergenerational effects of maternal malnutrition.

A double-blind study of Vietnamese children aged 6–24 months used a multimicronutrient supplement containing iron, zinc, retinol, and vitamin C given weekly or daily for 3 months. Only those children with severe linear growth retardation \( (i.e., \text{a height-for-age } z \text{ score of } -2 \text{ SD or greater}) \) had a positive response in linear growth (but not in weight gain) compared with their stunted placebo counterparts (130); no response was found in the supplemented compared with the placebo groups overall. No details are given of morbidity or of the nature and timing of complementary foods provided in this study.

In a recent Ghanaian study, breast-fed infants aged 6–12 months were randomly assigned to receive one of four foods: Weanimix; Weanimix fortified with vitamin A, iron, zinc, copper, calcium, phosphorus, and potassium (Group WM); Weanimix enriched with fish powder; and fermented maize porridge \( (i.e., \text{koko}) \) plus fish powder (131). Surprisingly, no significant differences in linear or ponderal growth or in biochemical micronutrient status were reported between intervention groups, with the exception of the absence of a significant increase in low serum ferritin values in the WM group compared with the other three groups, and a greater increase in plasma retinol in the WM group than in the other three groups combined. However, weight and length \( z \) scores of all four intervention groups were higher between 9 and 12 months of age than in nonintervention comparison infants, perhaps because of the provision of the complementary foods, their storage in vacuum flasks, or the weekly visits to the mothers.
In an attempt to establish whether zinc was the first growth-limiting nutrient, two trials have supplemented children with zinc plus a range of micronutrients and micronutrients alone (59,132). Of these, only the trial of Chinese schoolchildren by Sandstead and co-workers (132) showed a greater response in linear growth to zinc plus micronutrients than in those receiving the micronutrients alone. In a Guatemalan study by Cavan et al. (59), a pretreatment phase was also included, in which all participating children received a supplement of essential micronutrients (excluding zinc) in an effort to expose zinc as the only remaining deficiency (107).

Improving Dietary Quality with Micronutrient-Rich Foods or Fortificants

Instead of using multimicronutrient supplements, increases in the intake of several growth-limiting nutrients could be achieved simultaneously by enhancing the quantity as well as the dietary quality of the complementary diet through food-based approaches. Some of these are discussed below.

Several definitions are used to define diets of high dietary quality. Some are based on their content of available nutrients per unit energy, whereas others are based on greater dietary diversity or on the inclusion of foods from animal sources, resulting in increases in both micronutrient content and bioavailability. Several observational studies in a diverse cultural setting have shown a positive association between dietary diversity or quality and linear growth. For example, a study by Onyango et al. (133) of children aged 12–36 months found that dietary diversity (i.e., the number of different foods) was positively associated with height-for-age z score among partially breast-fed and weaned Kenyan children, even after controlling for sociodemographic variables. Indeed, height-for-age z score was greater in partially breast-fed children with a dietary diversity of more than five foods a day than in those consuming five or less foods a day ($-1.6 \pm 1.1$ vs. $-1.8 \pm 1.0, p < 0.05$). These results suggest that dietary diversity may serve as a proxy for dietary quality. Certainly, intakes of energy and several of the growth-limiting nutrients reported from non-breast-milk foods (e.g., protein, vitamin A, riboflavin, calcium, iron) for those infants who were partially breast-fed were significantly greater (as a percentage of Food and Agriculture Organization [FAO]/WHO dietary reference values) among those consuming complementary diets with a higher dietary diversity.

The quality of diets of Mexican toddlers (aged 18–30 months) in relation to linear growth was also examined in detail in the Nutrition CRSP study (9,134). These toddlers were fully weaned, and hence the results may not be directly applicable to partially breast-fed children. Nevertheless, similar foods are also used in complementary feeding in this geographic location. In this study, components associated with dietary quality were identified. Diets of high quality were defined as those containing more animal products, fruits, and milk (i.e., a greater variety of nonmaize foods), whereas those of low quality had a higher content of maize and beans. Attained height at 30 months was positively associated with energy intake from animal foods but negatively associated with energy intake from plant foods. Indeed, higher intakes of the maize-based staple tortilla (expressed as percentage of energy from tortillas) were
associated with reduced bioavailability of calcium, iron, and zinc, as indicated by total phytate, phytate/zinc molar ratios, and (phytate calcium)/zinc molar ratios, which in turn were negatively associated with height. These relations existed even after controlling for sociodemographic variables. By contrast, intakes of single nutrients were not significantly associated with attained height, with the notable exception of retinol. The latter, however, may have been a surrogate for animal food intakes. These results emphasize the importance of examining bioavailability variables as well as food consumption patterns when assessing dietary quality, particularly where staple foods are known to contain potent inhibitors of micronutrient bioavailability.

In a Peruvian study, Marquis et al. (135) assessed linear growth of partially breast-fed and fully weaned children between 12 and 15 months of age in relation to intake from animal foods. The diet-related variables, assessed by monthly food frequency questionnaires for 3 months, were frequency of breast-feeding, intake of complementary foods (number of food categories consumed), and number of animal source foods. Data for children with low linear growth rates and a high frequency of breast-feeding were excluded from the analysis; their situation was described as reverse causality. The poorer growth of these children arising from a high incidence of diarrhea was responsible for the mother’s decision to continue breast-feeding (136). Results indicated that the positive effect of a high intake of animal source foods on length gain over 3 months was significant only among children with low intakes of complementary foods (+0.2 cm) or those who were breast-fed infrequently (+0.4 cm). Also, linear growth was greater among those children with low intakes of animal source foods who were partially breast-fed (+0.5 cm) than in those who were fully weaned. Thus, in this population, both animal source foods and breast milk had significant positive effects on linear growth, but the effect of each was apparent only when other feeding behaviors were limiting.

Several intervention trials have also been conducted using a variety of food-based approaches to enhance the quality of complementary diets. These have included enrichment with various micronutrient-dense foods [e.g., meat, fish, eggs, or dairy products (137–139)], using germinated cereal flours to enhance the energy and nutrient densities (140), and augmenting the complementary diets with local snack foods (141) or high-energy, moderate-protein, micronutrient-fortified drinks (142,143). In some cases, specific feeding advice and cooking demonstrations rather than foods have been provided to caretakers in their homes (144).

To our knowledge, no trials have included methods designed to reduce the content of absorption inhibitors such as phytate in plant-based complementary foods, with the aim of enhancing the bioavailability of zinc, nonheme iron, and calcium. This is unfortunate because some simple home-based food preparation and processing methods—such as germination, fermentation, and soaking—can be used to reduce the phytate content of cereal/legume-based complementary foods by hydrolysis of phytate by phytase enzymes or diffusion of water-soluble phytate. Details of these low-technology household methods are summarized in Gibson and Ferguson (145). Studies are required to examine the impact of such modifications on linear (and ponderal) growth during the complementary feeding period.
The impact of some of the efficacy and effectiveness trials using fortificants or micronutrient-rich foods, drinks, or snacks to enhance dietary intakes from nonmilk foods and growth of infants aged 6–12 months has recently been reviewed by Caulfield et al. (146). Of the four efficacy studies in this review that measured energy intake, linear growth, and weight gain, all reported increases in energy intake from non-breast milk foods and a positive impact on linear (as well as ponderal) growth in the intervention group compared with the control group (137–139, 141–143), although in the Indonesian study, the change in height-for-age $z$ score was not significant (141). The design of these studies makes it difficult to attribute the changes observed directly to the improved complementary foods per se and specifically to changes in micronutrient intakes, because in no case was micronutrient intake quantified, and emphasis was also given on improving breast-feeding practices. In the two effectiveness trials reviewed by Caulfield et al. (146) that evaluated both changes in energy intake and linear growth (147, 148), significant increases in energy intake occurred in most age groups, which were associated with a positive impact on height-for-age $z$ scores of the infants. However, limitations noted in the efficacy trials were also present in these effectiveness trials.

These results indicate that complementary feeding interventions can result in improvements in linear growth during and after the complementary feeding period. Nevertheless, the design of these food-based studies and data collected in them make it impossible to establish which, if any, of the growth-limiting nutrients were improved in the diet and which ones were responsible for any improvements in linear growth observed.

In summary, there is some evidence that complementary diets of high quality—defined as those with a high proportion of energy from animal source foods or with a high content and bioavailability of micronutrients—can enhance linear growth during infancy in some circumstances. However, their impact on linear growth may be modulated by initial nutrient and growth status, diet type, total intake of complementary foods, presence of absorption inhibitors, mode of young child feeding (i.e., whether partially breast-fed or fully weaned), and constraints on growth associated with infection, the long-term effects of prenatal malnutrition, and intergenerational effects of maternal malnutrition. Hence, more carefully designed studies are required for adequate evaluation of the impact of dietary quality on linear growth and identification of the extent to which deficits in energy or specific growth-limiting nutrients are responsible for any changes in linear growth observed.

FUTURE RESEARCH ACTIVITIES AND CONCLUSIONS

More research is needed to identify the nutritional determinants of linear growth during the complementary feeding period specific to different ecological settings. With such information, improved country-specific complementary feeding strategies can be designed that have the potential to support normal growth and development during infancy and childhood.

To achieve this goal, more data are urgently needed on the composition of complementary foods consumed by infants of various ages in developing countries and at
different seasons as well as on the intake of micronutrients and antinutrients from these foods. Such data can then be compared with the estimated nutrient needs and desirable nutrient densities to determine the nutrient adequacy, and hence the quality, of complementary diets in diverse cultural settings.

The existence of any predicted nutrient inadequacies during complementary feeding must be confirmed using appropriate sensitive and specific biochemical indices. With use of these results, the extent to which any growth-limiting nutrient deficiencies are associated with impaired linear growth can be investigated, taking into account any confounding variables such as morbidity and so on. Next, based on this evidence, a series of double-blind placebo-controlled trials involving different combinations of micronutrient supplements specific to each ecological setting should be conducted. These trials should be randomized, and with a design, sample size, age group, and length of study period that will enable the effect of the first limiting nutrient on linear growth to be evaluated in the absence of any confounding co-existing micronutrient deficiencies. Only in this way can the contribution of each growth-limiting nutrient to linear growth retardation during the complementary feeding period be elucidated.

Research must also be conducted at the local household level to improve the content and bioavailability (i.e., dietary quality) of micronutrients known to be limiting in complementary diets and to evaluate the impact of such improvements on linear growth and morbidity. Even if these strategies are employed, however, they may not be sufficient to overcome the deficits in iron and zinc that are so often present in plant-based complementary foods. Consequently, research on the feasibility of fortifying plant-based complementary foods with protected fortificants containing balanced and physiological levels of micronutrients specific to the cultural setting, and possibly also added commercial amylase and phytase enzymes, is urgently required. In developing countries, where the use of centrally processed fortified complementary foods is not feasible, micronutrient sachets, possibly with added amylase and heat-stable phytase enzymes, may be a feasible strategy. These could be added to complementary foods by rural mothers, although quality assurance issues need to be addressed.

The use of the systematic approach outlined above will enable complementary foods to be designed to optimize linear growth during infancy and early childhood in various cultural settings. Nevertheless, enhancing complementary diets must also be accompanied by improvements in maternal nutritional status, socioeconomic status, and education as well as by reductions in morbidity before optimal linear growth can be achieved.

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**DISCUSSION**

*Dr. Haschke:* I was puzzled by your estimate of the requirement for zinc. You indicated that 95% of the zinc for a 9- to 11-month-old infant should come from complementary foods; that means that only 5% would come from breast milk. If we consider that breast milk has a zinc content of 4 mg/l and the child is drinking between 250 and 500 ml, that would indicate an intake of 1–2 mg/day from breast milk alone.
The daily requirement for zinc is 4 mg, so only 2 mg is missing. WHO calculated that 95% should come from complementary foods?

Dr. Gibson: It depends on which estimate you use for zinc requirements, and this is still a much debated issue. The WHO estimate is derived from their 1996 data and is considerably higher than that given by Krebs and Hambidge (1) and Krebs et al. (2). The particular example I gave you was calculated for infants 9–11 months of age using the WHO estimate. We also need to remember that the zinc content of breast milk declines quite rapidly during lactation, and there is certainly evidence that infants from 6 months of age do require an additional source of zinc. Maybe 98% is an overestimate, but nevertheless, a large proportion of the zinc intake does have to come from complementary foods after 6 months of age.

Dr. Haschke: There is a difference between sitting in an office in Rome or Washington, DC, and calculating the zinc intakes of the US population or the European population, and actually applying these calculations in the field in developing countries. It is difficult to achieve the intake suggested here with normal foods or even with enriched foods. One should be very careful about following these recommendations blindly. It’s possible to achieve these target intakes by giving supplements, but that is not a natural way to provide food for infants. What is achievable should be very much in the context of what is effective, and we have no idea whether or not a zinc intake of 2 mg is sufficient to ensure normal growth, as the studies to show this are lacking. We are just taking recommendations from the Western world and transferring them to the developing countries. That is my main criticism.

Dr. Gibson: I recognize the limitations of this approach, but it is a start. There is certainly more controversy about zinc requirements than there is for most other nutrients, but the meta-analysis of Brown et al. (3) did show that zinc supplementation during infancy and childhood had an impact on growth. Thus, there is some suggestion from double-blind zinc intervention studies that infants in both developing and developed countries are not necessarily obtaining the optimal amounts of zinc for their needs.

Dr. Rivera-Dommarco: You presented some preliminary data from our supplementation study in Mexico. We have now finished the analyses, and we found that the overall effect of multiple micronutrients was about the same as you just presented. But when we looked at interactions, we found that the effect was restricted to children less than 12 months of age. The effect on those children was +0.30 of the SD in length for supplementation over a 1-year period, and there was no effect on children older than 12 months. So, the effect is important in younger children.

Dr. Gibson: Thank you very much. That once again suggests that the younger age group is particularly at risk.

Dr. Uauy: You have been trying a food-based approach at field level, especially flesh foods, but how realistic is that? Although food-based approaches are always favored, in practice, we all promote fortified foods as a way of providing micronutrients.

Dr. Gibson: In the area where I have been working, rural Malawi, the addition of substantial amounts of flesh foods to the diet is not an option because the resources available to the mothers are very limited. So, our aim was to try to improve the content and bioavailability of micronutrients in available complementary foods. Our main strategy was not to increase flesh foods—although we did advocate the use of fish powder whenever possible—but to reduce the hexa- and pentainositol phosphate
content of maize-based complementary foods by soaking the pounded maize before it was ground. This was a strategy that the mothers readily adopted. You can reduce the hexa- and pentainositol phosphate content of maize-based porridges by 50% using this simple procedure. However, even when you reduce the hexa- and pentainositol phosphate content using these methods and simultaneously increase the zinc content by enriching the complementary foods with a small amount of flesh foods, that was still not enough to meet the estimated needs for iron and zinc. That is why I concluded, based on this particular small study in Malawi where mothers have very limited local resources, that we may have to consider fortification of complementary foods for certain nutrients.

Dr. Ramakrishnan: In the study in Mexico that Dr. Rivera-Dommarco referred to, one of our students followed up the children, and—much to our dismay—we found that after about a year, those who had the initial benefit regressed and the differences disappeared. The point I want to make is that it may be unrealistic to expect benefits, even from multiple micronutrients, when the intervention is only given for a short time. In our present Mexican study, we are providing multiple micronutrient supplements to pregnant women and then to randomized children right through to 2 years of age. We hope this will be long enough to have a long-lasting effect.

Dr. Gibson: That’s a very important point. It emphasizes the fact that if we can use a food-based approach that is sustainable, so that mothers continue to use it every day while their children are growing up, then at least we may be able to improve the baseline nutritional status of those children and give them a better chance later on, whether or not they have access to supplements.

Dr. Bhan: When you look at the size of the effect of individual micronutrients as well as of multiple micronutrients, I think you would agree that it is quite small. Does that tell us that the level of deficiency that we see in these populations is unlikely to have a critical effect on growth? Animal data are not very helpful here, as most reflect the severe end of the spectrum of deficiency.

Dr. Gibson: I believe these nutrients play an important role in growth, but this may not be shown by single-nutrient short-term intervention trials. There are many other factors that affect linear growth besides these limiting nutritional factors, and if a mother is small to start with, and there are problems with intrauterine growth retardation, it’s going to take a long time to show an improvement. That does not mean that we should not try to improve nutritional status at the same time as trying to reduce morbidity and improve socioeconomic status.

Dr. Bhan: We also need to examine the impact of these supplements on functions other than growth, and I’m referring particularly to infection. The low-birthweight trial in India seems to suggest that the benefit of zinc on infection and survival is lost when multiple micronutrients are given instead, perhaps because some of the micronutrients are driving the immune response in a particular direction, probably altering the TH1/TH2 balance, while others are working in the opposite direction. We don’t fully understand what is happening here, but it seems clear that multiple micronutrients do not have the same impact on infection as zinc—which as you know is substantial. I think that dimension needs to be taken into account in the overall picture.

Dr. Gibson: We still are not sure about the multiple micronutrient interactions that may take place. In some cases, the multiple micronutrient supplements that we are providing are not in optimal physiological balance. In other cases, the supplement
s lens that have been used aren’t readily available in the presence of high-phytate diets. Thus, there may be occasions when the impact of the micronutrient supplement mix may not be optimal, and we need to take that into account.

Dr. Uauy: One of the problems with micronutrient fortification or supplementation trials is that they are usually applied to the whole population. It is assumed that all stunted children are micronutrient deficient. We also have the problem of potential toxicity. Within that framework, I think that we ought to be putting more emphasis on trying to develop simple methods of identifying zinc deficiency. We cannot equate stunting with micronutrient deficiency and then just throw in micronutrients. How would you approach this on a practical basis? Can we target those who will benefit by a screening procedure?

Dr. Gibson: As you know, the big problem with zinc is that we do not have a readily available specific biochemical index for detecting zinc deficiency. Plasma zinc may be useful on a population basis, but on an individual basis, it is much less useful. I think there are indicators that we can use—particularly from the diet—that may give us a clue about whether or not certain micronutrient deficiencies are going to be present in a population subgroup, taking into account, for instance, the proportion of energy that comes from flesh- versus plant-based products and the amount of phytate in the diet. The phytate/zinc and the phytate/iron molar ratios can certainly provide us with some information about the potential bioavailability of these two micronutrients. So, I think we should look at the prevalence of stunting, at the composition of the base diet, and at the prevalence of infection. Such a combination may provide us with some information about whether or not a particular micronutrient is likely to be deficient, until we are at a stage where we have better screening tools, especially for zinc.

Dr. Cassorla: May I make a contribution as an endocrinologist? I’m a little worried about interventions during this period of life when children are attempting to reach their genetic potential in terms of growth. This is a time when there are various shifts in growth channels, particularly those based on the genetic background. Do these studies include measurements of the parents? It does not seem that this would be a very complicated thing to do, but I think it would add a lot. If you have tall parents, you are likely to have a shift upward during this period; if you have short parents, you are likely to have a downward shift. It shouldn’t be that difficult to gather such information and incorporate it into these trials.

Dr. Gibson: Some trials have included parental height, but not all. It’s something we should routinely include.

Dr. Gomez: Could you comment on the use and effects of commercially available multivitamin preparations in relation to linear growth? In our country, it is common practice to give these in addition to micronutrient supplements in complementary foods and beverages.

Dr. Gibson: The vitamin literature I examined was mainly associated with the single-nutrient intervention trials of vitamin A. As far as I am aware, there are no single-nutrient vitamin supplementation trials of riboflavin or vitamin B12, nor of multivitamins, which have examined an effect on linear growth, so I am unable to answer that question. I’m not familiar with that literature.

Dr. Castillo: What about the interactions between calcium and zinc? Calcium deficiency may protect against zinc deficiency. In some programs, when we improve calcium nutrition, we may increase zinc deficiency.
Dr. Gibson: I'm familiar with the interaction between calcium and zinc in the presence of high levels of phytate, and certainly if I were designing a multimicronutrient supplementation trial and considering including calcium, I would be very concerned about the level of calcium that was added in relation to the negative effect it might have on zinc absorption.

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