ZINC NUTRITION IN DEVELOPING COUNTRIES

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INTRODUCTION

Recently the United Nations has urged that priority should be given to developing programmes in less industrialized countries to prevent deficiencies of iodine, vitamin A, and Fe (United Nations, 1991). Nutritional Fe deficiency is associated with plant based diets which contain high levels of dietary fibre and phytate, components known to inhibit non-haem Fe absorption, and low levels of flesh foods, rich sources of readily available haem iron (Monsen, 1988). Such plant based diets will also induce Zn deficiency. The consequences of Zn deficiency on human health in developing countries, however, have not yet been recognized. This is unfortunate because even mild Zn deficiency may contribute to pregnancy complications, low birth weight, impaired immune competence, maternal and infant mortality and morbidity, and growth failure in infancy and childhood (Swanson & King, 1987; Hambridge, 1989; National Academy of Sciences, 1991; United Nations, 1991). Hence Zn deficiency may have far reaching consequences on maternal, infant, and child health in many developing countries.
Table 1. Zinc†, phytic acid† and [phytate]:[zinc] molar ratios of some foods and composite dishes consumed in Ghana and Malawi

<table>
<thead>
<tr>
<th>Food, and scientific name or recipe</th>
<th>Zn</th>
<th>Phy</th>
<th>Phy:Zn</th>
<th>% H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cereals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maize flour, 95% extraction (Zea mays L.)</td>
<td>2.2</td>
<td>792</td>
<td>36</td>
<td>10</td>
</tr>
<tr>
<td>Maize flour, 65% extraction</td>
<td>0.9</td>
<td>211</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>Maize bran</td>
<td>3.7</td>
<td>1089</td>
<td>29</td>
<td>10</td>
</tr>
<tr>
<td>Maize dough</td>
<td>1.4</td>
<td>n.a.</td>
<td>n.a.</td>
<td>50</td>
</tr>
<tr>
<td>Sorghum flour (Sorghum bicolor (L.) Moench)</td>
<td>1.4</td>
<td>446</td>
<td>32</td>
<td>10</td>
</tr>
<tr>
<td>Rice (Oryza sativa)</td>
<td>1.6</td>
<td>n.a.</td>
<td>n.a.</td>
<td>10</td>
</tr>
<tr>
<td>Legumes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ground nuts, boiled (Arachis hypogaea L.)</td>
<td>1.4</td>
<td>505</td>
<td>35</td>
<td>49</td>
</tr>
<tr>
<td>Ground nuts, flour</td>
<td>2.8</td>
<td>1297</td>
<td>45</td>
<td>8</td>
</tr>
<tr>
<td>Pigeon peas, fresh ( Cajanus cajan (L.) Millsp.)</td>
<td>0.9</td>
<td>255</td>
<td>27</td>
<td>63</td>
</tr>
<tr>
<td>Pigeon peas, dry</td>
<td>2.2</td>
<td>727</td>
<td>33</td>
<td>8</td>
</tr>
<tr>
<td>Kidney beans, fresh (Phaseolus vulgaris L.)</td>
<td>1.5</td>
<td>557</td>
<td>36</td>
<td>52</td>
</tr>
<tr>
<td>Cowpeas, boiled (Vigna unguiculata (L.) Walp.)</td>
<td>1.0</td>
<td>349</td>
<td>37</td>
<td>68</td>
</tr>
<tr>
<td>Lima beans, fresh (Phaseolus lunatus L.)</td>
<td>1.5</td>
<td>238</td>
<td>16</td>
<td>66</td>
</tr>
<tr>
<td>Bengal beans, fresh (Stizolobium aterrimum Piper &amp; Tracey)</td>
<td>1.0</td>
<td>166</td>
<td>17</td>
<td>68</td>
</tr>
<tr>
<td>Vegetables (boiled)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pumpkin leaf (Cucurbita maxima Duch. ex Lam.)</td>
<td>0.7</td>
<td>34</td>
<td>5</td>
<td>89</td>
</tr>
<tr>
<td>Chinese cabbage (Brassica chinensis L.)</td>
<td>0.7</td>
<td>5</td>
<td>1</td>
<td>94</td>
</tr>
<tr>
<td>Okra leaf (Hibiscus esculentus (L.))</td>
<td>1.8</td>
<td>97</td>
<td>5</td>
<td>79</td>
</tr>
<tr>
<td>Okra (Hibiscus esculentus (L.))</td>
<td>0.5</td>
<td>13</td>
<td>3</td>
<td>91</td>
</tr>
<tr>
<td>Cassava leaf (Manihot esculenta Crantz)</td>
<td>1.2</td>
<td>42</td>
<td>3</td>
<td>78</td>
</tr>
<tr>
<td>Cocoyam leaves (Xanthosoma sp. Schott.)</td>
<td>0.6</td>
<td>19</td>
<td>3</td>
<td>88</td>
</tr>
<tr>
<td>Amaranth leaves (Amaranth sp. L.)</td>
<td>0.3</td>
<td>n.a.</td>
<td>n.a.</td>
<td>93</td>
</tr>
<tr>
<td>Roots and plantain (boiled)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweet potato (Ipomoea batatas L.)</td>
<td>0.2</td>
<td>10</td>
<td>5</td>
<td>70</td>
</tr>
<tr>
<td>Yam (Dioscorea sp. L.)</td>
<td>0.3</td>
<td>50</td>
<td>13</td>
<td>68</td>
</tr>
<tr>
<td>Cocoyam (Xanthosoma sp.)</td>
<td>0.5</td>
<td>37</td>
<td>7</td>
<td>60</td>
</tr>
<tr>
<td>Cassava (Manihot sp.)</td>
<td>0.3</td>
<td>54</td>
<td>18</td>
<td>65</td>
</tr>
<tr>
<td>Cassava dough, fermented</td>
<td>0.4</td>
<td>48</td>
<td>12</td>
<td>51</td>
</tr>
<tr>
<td>Gari: dry fermented cassava, not boiled</td>
<td>0.7</td>
<td>51</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Plantain, ripe (Musa paradisiaca L.)</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
<td>73</td>
</tr>
<tr>
<td>Plantain, unripe (Musa paradisiaca L.)</td>
<td>0.2</td>
<td>1</td>
<td>1</td>
<td>65</td>
</tr>
<tr>
<td>Water yam (Dioscorea alata L.)</td>
<td>0.2</td>
<td>26</td>
<td>16</td>
<td>72</td>
</tr>
<tr>
<td>Fruits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avocado pear (Persea americana Mill.)</td>
<td>0.3</td>
<td>11</td>
<td>3</td>
<td>78</td>
</tr>
<tr>
<td>Banana (Musa paradisiaca L.)</td>
<td>0.2</td>
<td>22</td>
<td>9</td>
<td>72</td>
</tr>
<tr>
<td>Mango, raw (Mangifera indica L.)</td>
<td>0.1</td>
<td>25</td>
<td>23</td>
<td>82</td>
</tr>
<tr>
<td>Composite dishes – home-prepared snacks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chitumbuwa (mixture of water, maize flour and pounded bananas formed into a round cake and fried in oil)</td>
<td>1.2</td>
<td>504</td>
<td>42</td>
<td>30</td>
</tr>
<tr>
<td>African bread (mixture of water, maize flour and bananas formed into a cake, wrapped in banana leaves and boiled until cooked)</td>
<td>0.3</td>
<td>102</td>
<td>37</td>
<td>70</td>
</tr>
<tr>
<td>African cake (mixture of water, maize flour and sugar baked in tin can)</td>
<td>1.2</td>
<td>297</td>
<td>26</td>
<td>45</td>
</tr>
<tr>
<td>Composite dishes – staples</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hausa porridge (thin porridge of corn flour)</td>
<td>0.1</td>
<td>25</td>
<td>25</td>
<td>94</td>
</tr>
<tr>
<td>Porridge of corn grits</td>
<td>0.1</td>
<td>23</td>
<td>23</td>
<td>88</td>
</tr>
<tr>
<td>Banku (boiled mixture of corn dough and cassava dough)</td>
<td>0.7</td>
<td>107</td>
<td>16</td>
<td>73</td>
</tr>
<tr>
<td>Ga kenkey (corn dough made into dumplings and boiled in banana leaves)</td>
<td>0.8</td>
<td>172</td>
<td>19</td>
<td>71</td>
</tr>
<tr>
<td>Fanti kenkey (corn dough made into dumplings and boiled in plantain leaves)</td>
<td>0.7</td>
<td>118</td>
<td>21</td>
<td>72</td>
</tr>
<tr>
<td>Fufu (pounded boiled cassava and plantain)</td>
<td>0.4</td>
<td>96</td>
<td>24</td>
<td>69</td>
</tr>
<tr>
<td>Composite dishes – purchased meals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 1 (cont.)

<table>
<thead>
<tr>
<th>Food, and scientific name or recipe</th>
<th>Zn</th>
<th>Phy</th>
<th>Phy:Zn</th>
<th>% H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice and stew (rice and standard ingredients†)</td>
<td>0.6</td>
<td>118</td>
<td>21</td>
<td>68</td>
</tr>
<tr>
<td>Rice and beans (rice, cowpeas and standard ingredients)</td>
<td>0.5</td>
<td>107</td>
<td>18</td>
<td>70</td>
</tr>
<tr>
<td>Gari and beans (gari, cowpeas and standard ingredients)</td>
<td>0.9</td>
<td>178</td>
<td>22</td>
<td>59</td>
</tr>
<tr>
<td>Composite dishes – soups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palmnut soup (water, palmnut cream and standard ingredients)</td>
<td>0.4</td>
<td>n.a.</td>
<td>n.a.</td>
<td>86</td>
</tr>
<tr>
<td>Groundnut soup (water, groundnut paste and standard ingredients)</td>
<td>0.8</td>
<td>81</td>
<td>10</td>
<td>88</td>
</tr>
<tr>
<td>Composite dishes – stews</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Okra (okra and standard ingredients)</td>
<td>0.4</td>
<td>38</td>
<td>9</td>
<td>90</td>
</tr>
<tr>
<td>Bean (cowpeas and standard ingredients)</td>
<td>0.7</td>
<td>n.a.</td>
<td>n.a.</td>
<td>72</td>
</tr>
</tbody>
</table>

†, mg/100 g wet weight. n.a., not analysed.
‡, standard ingredients: tomato, red peppers, salt, onion, fish; palm oil in stews, rice and beans, and gari and beans.
Phy:Zn, [phytate]/[Zn] molar ratios. Phytate was analysed by the standard AOAC method (Harland & Oberleas, 1986).
All data from Ferguson et al. (1988, 1989b, 1993a).

AETIOLOGY OF ZINC DEFICIENCY IN DEVELOPING COUNTRIES

DIETARY FACTORS: LOW INTAKE AND POOR BIOAVAILABILITY OF DIETARY ZINC

The nutritional adequacy of dietary Zn depends on both its amount and bioavailability in the diet. Flesh foods are a rich source of Zn which is readily available because during their digestion certain L-amino acids and cysteine-containing peptides are released, which form soluble ligands with Zn (Sandström et al. 1980, 1989). In many developing countries, however, the content of flesh foods in rural diets is often low so that their contribution to total dietary Zn intake is small. Instead, diets are mainly plant based; cereals, starchy roots and/or tubers are often the major sources of Zn in rural diets. Of these staples, starchy roots and tubers generally have a lower Zn content than cereals, as shown by the Ghanaian and Malawian examples shown in Table 1. Hence, diets based on these staples tend to be correspondingly lower in Zn than cereal based diets (Gibson et al. 1991a; Ferguson et al. 1993a). Nevertheless, in certain geographical areas where Zn deficient soils exist, cereal staples will have a lower Zn content than when grown on Zn sufficient soils.

Plant based diets often contain high levels of phytic acid (myoinositol hexaphosphate) and dietary fibre, components known to inhibit the absorption of dietary Zn (Sandström, 1989). Of these antinutrients, phytic acid (Phy), the major storage form of phosphorus in cereals, legumes, and oleaginous seeds, is the most potent inhibitor of Zn absorption (Sandström & Lönnnerdal, 1989). It forms insoluble chelates at a physiological pH. The lower inositol phosphates (i.e. tetra-, tri-, di-, and mono-inositol phosphates), formed by enzymic or non-enzymic hydrolysis of phytic acid, do not form insoluble complexes with Zn (Lönnnerdal et al. 1989). The bioavailability of dietary Zn can be predicted from the ratio of phytic acid [Phy] to zinc [Zn] in diets. The critical [Phy]:[Zn] molar ratios associated with risk of Zn deficiency are equivocal; ratios above 15 have been associated with biochemical (Harland & Peterson, 1978; Oberleas & Harland, 1981; Turnlund et al. 1984; Bindra et al. 1986), and in some cases clinical signs of Zn deficiency in humans (Ferguson et al. 1989a).
Plant based staples such as unrefined maize flour, brown rice, sorghum and certain legumes (e.g. groundnuts, pigeon peas, kidney beans, and cowpeas) have elevated [Phy]:[Zn] molar ratios (Table 1; Ferguson, 1992). Hence, diets based on cereals and legumes have higher [Phy]:[Zn] molar ratios than those based on starchy roots and/or tubers (Ferguson et al. 1993a; Fitzgerald et al. 1993).

High levels of calcium potentiate the inhibitory effect of phytate on Zn absorption by forming a Ca:Zn:phytate complex that is even less soluble than phytate complexes formed by either ion alone (Wise, 1983). Hence, some authors have proposed that dietary [Phy][Ca]:[Zn] ratios may be a better predictor of Zn bioavailability than [Phy]:[Zn] ratios alone (Davies et al. 1985; Fordyce et al. 1987). To date, the critical [Ca][Phy]:[Zn] molar ratio that compromises Zn bioavailability in human diets has not been clearly defined. Retrospective calculations of experimental data from Cossack & Prasad (1983) suggest that molar ratios above 0.2 (200 mmol) may be associated with decreased Zn bioavailability in human diets. Most plant based diets are low in Ca, however, with the exception of those based on tortillas (Fitzgerald et al. 1993). The latter contain a relatively high concentration of Ca, derived from lime used to soak the maize in the preparation of nixtamal (soaking of corn kernels to liberate the husks) before being milled into masa (raw corn dough). Diets of lacto-ovo vegetarians may also have elevated [Ca][Phy]:[Zn] molar ratios (Bindra et al. 1986).

Dietary fibre, notably the insoluble fibres cellulose and lignin, may also inhibit Zn absorption to some degree, although their effects are equivocal, in part because fibre generally occurs concomitantly with phytic acid, making any independent inhibitory effect difficult to establish (Torre et al. 1991).

The bioavailability of Zn can also be affected by competitive interactions among certain micronutrients in the intestine, notably between Zn and non-haem Fe, and Zn and copper (Mills, 1985). The Fe and Cu contents of most human diets, however, are generally not high enough to compromise Zn bioavailability, unless high doses of supplemental non-haem iron are used (Solomons, 1986). In some cases, a negative Fe–Zn interaction has not been observed when the Fe is mixed with or is present as an intrinsic part of a food or meal (Valberg et al. 1984). Some (Milhe et al. 1984; Mukherjee et al. 1984) but not all (Butterworth et al. 1988; Krebs et al. 1988) researchers have also observed a negative effect of high doses of folate supplements on Zn status, which could be of significance for pregnant women prescribed both supplemental folate and non-haem iron.

**EXCESSIVE LOSSES**

Additional factors that may exacerbate suboptimal Zn status in population groups living in developing countries include increased endogenous losses of Zn through perspiration; exfoliation of the skin as a result of the hot, humid climate; chronic haemolysis due to genetic factors (e.g. α-thalassaemia, sickle cell disease) and/or parasite infections (e.g. malaria, hookworm, schistosomiasis), and diarrhoea (Solomons, 1981; Ruz & Solomons, 1990). Ferguson (1992) estimated urinary Zn losses from haemolysis induced by schistosomiasis to range from 0·02 to 0·85 mg/d; faecal losses of Zn in infants with chronic diarrhoea can be as high as 300 μg/kg daily (Rothbaum et al. 1982). In areas where geophagia is practised, extensive faecal losses arising from poor absorption of dietary Zn may exacerbate Zn deficiency (Prasad et al. 1963).

**HIGH PHYSIOLOGICAL REQUIREMENTS**

The FAO/WHO/ILEA committee are currently revising the Zn requirements to include estimates to meet both basal and normative requirements (FAO/WHO/ILEA, un-
published observations, 1992). Basal requirements are the amount needed to prevent clinically detectable signs of functional impairment whereas the normative requirement represents the amount needed to maintain tissue stores or reserve capacity.

Physiological requirements of Zn are increased during periods of rapid growth because it has such a critical role in nucleic acid synthesis and protein metabolism. Hence, infants and children are especially vulnerable to Zn deficiency. In infants in developing countries, Zn stores at birth may be small as a consequence of their low birth weight and poor nutritional status of the mothers. Therefore, their dietary requirements for catch-up growth will be higher than those of infants from industrialized countries.

Male infants and children appear to have higher requirements for Zn than females, because of their higher growth rates and greater proportion of muscle/kg body weight; muscle contains a higher content of Zn than fat (Giugliano & Millward, 1984). In several double-blind supplementation studies, males have exhibited greater improvements in rate of linear growth and/or weight gain than their Zn supplemented female counterparts (Walravens & Hambidge, 1976; Walravens et al. 1983, 1989; Castillo-Duran et al. 1987; Schlesinger et al. 1992; M. Ruz, 1993, pers. comm.).

Requirements for Zn are also greater during pregnancy and lactation for the growth and development of the fetus and maternal tissues, and secretion of breast milk. The FAO/WHO/ILEA committee (unpublished, 1992) calculated the average individual physiological requirements for absorbed Zn during each trimester of pregnancy to be 0·8, 1·0, 1·4 mg/d for the basal requirements and 1·1, 1·4, and 2·0 mg/d for the normative requirements. These estimates do not take into account differences in the absorbability of dietary Zn or the varied intakes within the population. During the course of lactation, Zn concentrations in human milk decline (Casey et al. 1989). Hence, estimates of the average individual basal requirement range from 1·6 at 0–3 months and 1·5 at 3–6 months to 1·2 mg/d between 6 and 12 months; corresponding estimates for normative requirements are 1·9, 1·8, and 1·5 mg/d respectively (FAO/WHO/ILEA, unpublished observations, 1992).

### ZINC INTAKES IN RELATION TO ESTIMATED REQUIREMENTS

In many developing countries, information on intakes and major food sources of Zn in local diets, as well as on the antinutrients dietary fibre and phytate, are limited, in part because of the paucity of data on the content of Zn and antinutrients in local foodstuffs. This is unfortunate because such data are essential for assessing the risk for inadequate intakes of dietary Zn, and for planning dietary strategies to improve its content and bioavailability in traditional diets.

Population groups consuming diets based predominantly on unrefined maize and rice generally have markedly higher intakes of phytate and elevated [Phy]:[Zn] molar ratios compared to those consuming diets based on starchy roots and/or tubers (Table 2) (Mbofung & Atinmo, 1987; Gibson et al. 1991a; Ferguson et al. 1993b; Fitzgerald et al. 1993). The latter, however, often have lower Zn intakes. Molar ratios of [Ca][Phy]:[Zn] in most of these plant based diets are low with the exception of those based on tortillas (Fitzgerald et al. 1993).

The adequacy of dietary Zn intakes can be evaluated by comparison with the newly revised requirements, provided an estimate of the bioavailability of Zn in the diet can be made. Diets can be categorized as high, moderate, or low in terms of Zn bioavailability, based on their content of animal or fish protein, calcium, and [Phy]:[Zn] molar ratios (FAO/WHO/ILEA, unpublished observations, 1992). Alternatively, more direct measure-
Table 2. Dietary intakes (mean ± sd) of zinc, phytate, phytate:zinc molar ratios, and dietary fibre of children in some developing countries

<table>
<thead>
<tr>
<th>Country (n) Age in years</th>
<th>Reference</th>
<th>Zinc (mg/day)</th>
<th>Phytate (mg/day)</th>
<th>Phy:Zn</th>
<th>Dietary fibre (g/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papua New Guinea (67) 6-10</td>
<td>Gibson et al. 1991a</td>
<td>4.4±1.3</td>
<td>646±663</td>
<td>12</td>
<td>37.1±11.4</td>
</tr>
<tr>
<td>Malawi (67) 4-6</td>
<td>Ferguson et al. 1993b</td>
<td>6.6±1.7</td>
<td>1899±590</td>
<td>25</td>
<td>24.9±6.4†</td>
</tr>
<tr>
<td>Ghana (148) 3-6</td>
<td>Ferguson et al. 1993b</td>
<td>4.7±1.1</td>
<td>591±153</td>
<td>13</td>
<td>15.5±3.8†</td>
</tr>
<tr>
<td>Egypt (96) 1.5-2.5</td>
<td>Murphy et al. 1992</td>
<td>5.2±1.6</td>
<td>796±249</td>
<td>16</td>
<td>17.4±5.9</td>
</tr>
<tr>
<td>Kenya (100) 1.5-2.5</td>
<td>Ferguson et al. 1993b</td>
<td>3.7±0.9</td>
<td>1066±324</td>
<td>28</td>
<td>21.6±5.5</td>
</tr>
<tr>
<td>Mexico (59) 1.5-2.5</td>
<td>Murphy et al. 1992</td>
<td>5.3±1.3</td>
<td>1666±650</td>
<td>30</td>
<td>15.3±4.8</td>
</tr>
<tr>
<td>Guatemala (136) 6-8</td>
<td>Murphy et al. 1992</td>
<td>9.0†</td>
<td>962†</td>
<td>11</td>
<td>14.0†</td>
</tr>
<tr>
<td>Canada (106) 4-6</td>
<td>Cavan et al. 1993a</td>
<td>6.9±2.3</td>
<td>(300)‡</td>
<td>5</td>
<td>11.4±5.5</td>
</tr>
</tbody>
</table>

† Non-starch polysaccharide.
‡ Median.

Measurements of the bioavailability of Zn in local diets can be made by using radioactive or stable isotope techniques (Sandström & Lönnend, 1989).

Some studies report average Zn intakes for a specific population group (Mbofung & Atinmo, 1987), often based on one day's intake per individual. Such data do not take into account the distribution of intakes among individuals and cannot be used to estimate the proportion of individuals within the population at risk for nutrient inadequacy. For the latter, food intake data based on at least two days' intake per person are required. If single days are used, prevalence estimates for risk of inadequacy are always too high (Beaton, 1985). To improve the reliability of the prevalence estimates for dietary inadequacy, they should be determined using the probability approach recommended by the Subcommittee for Criteria for Dietary Evaluation (National Research Council, 1986). When this approach has been used in studies of dietary Zn intakes of children in developing countries, a very high proportion of the children studied from Kenya and Malawi (> 90%), and more than two-thirds from Mexico and Ghana, were apparently at risk, assuming that the estimates used for both the bioavailability and basal requirements for Zn are valid (Murphy et al. 1992; Ferguson et al. 1993b).

Even the Zn intakes of exclusively breast fed infants may be inadequate during the first 4-6 months in some developing countries, especially if the infants are preterm and/or of low birth weight with high nutrient demands for catch-up growth. Moreover, their supply of Zn from breast milk may be compromised by the poor nutritional status of the lactating mothers, which may result in breast milk with an inherently low Zn content (Butte et al. 1992; Dorea, 1993) and/or low volume (Brown et al. 1986). To date, studies of the Zn concentrations of breast milk in poorly nourished lactating women with chronically inadequate Zn intakes have revealed inconsistent results. In some, breast milk Zn concentrations have been consistent with those reported for developed countries, and independent of maternal dietary Zn intakes (Kirsten et al. 1985; Karra et al. 1986; Moser et al. 1988; Simmer et al. 1990); others dispute this finding (Krebs et al. 1985; Shrimpton et al. 1985).
In many developing countries, breast milk output may also be compromised by the early introduction of weaning foods which replace rather than complement breast milk (Walker, 1990). Very often these weaning foods are prepared as thin porridges from staples with a low energy and nutrient density which fail to make up the nutrient deficit when breast milk no longer meets the infants’ needs. If unrefined and unfermented cereals and/or legumes are used, the weaning foods will have a high phytic acid content; consequently Zn bioavailability will be low. During fermentation, hexa- and penta-inositol phosphates are hydrolysed enzymically to the lower inositol phosphates which do not inhibit Zn absorption (Lönnerdal et al. 1989). More work is required in developing countries to evaluate the adequacy of dietary Zn intakes for both exclusively breast fed infants and for weanlings. To date, no recommendations for the Zn content of weaning foods in developing countries exist (Royal Tropical Institute, Amsterdam, 1987). This is unfortunate because Zn deficiency impairs appetite, taste acuity, immune and intestinal function during infancy (Hambidge et al. 1972; Krebs et al. 1984; Castillo-Duran et al. 1987; Roy et al. 1992; Schlesinger et al. 1993; Tomkins et al. 1993) as well as growth (Hambidge, 1989). Such functional disturbances will have a further detrimental effect on the growth and development of the infants.

A high proportion of pregnant women from developing countries are probably also at risk through inadequate intakes of Zn. Although no data based on the probability approach are available in the literature, in a Guatemalan study 94 and 25% of the pregnant women had average Zn intakes below or less than two-thirds of the US Recommended Dietary Allowance for Zn (15 mg) respectively, assuming that 20% of Zn was absorbed from their diets. Mean Zn intakes for pregnant rural and urban women in Nigeria were 6.0 and 6.7 mg/d, respectively, whereas during lactation they ranged from 7.3 to 8.2 mg/d for rural women (Mbofung & Atinmo, 1987). Corresponding mean intakes for Nepalese (Moser et al. 1988) and Amazonian (Jackson et al. 1988) lactating women were 10.5 and 8.8 mg Zn/d respectively.

Comparison of Zn intakes with the current estimated requirements does not take into account the possibility that humans can adapt to chronically low Zn intakes and achieve Zn balance by increasing Zn absorption (King, 1986). Certainly, Amazonian lactating women maintained normal Zn balance in the presence of low intakes of Zn (and phytate) (Jackson et al. 1988), although there was evidence of functional impairment because breast milk Zn and retinol contents were abnormally low. Whether such adaptation also occurs in the presence of very high habitual intakes of phytate seems unlikely. Brune et al. (1989) reported that vegetarians did not adapt to their high phytate diet by increased absorption of $^{59}$Fe.

Probability estimates for risk of Zn inadequacy do not identify actual individuals in the population who are deficient, or define the severity of the nutrient inadequacy. Such information can only be obtained when the dietary intake data are combined with laboratory and/or clinical indices of Zn status. This is especially important in developing countries where the coexistence of many other multifaceted health problems often confounds the diagnosis of Zn deficiency.

LABORATORY ASSESSMENT OF ZINC STATUS

BIOCHEMICAL INDICES OF ZINC STATUS

To date, no single, sensitive and specific index of Zn status exists (Golden, 1989). Serum/plasma Zn is the most frequently used index in human studies because it can be easily and accurately measured. Nevertheless, this index has several limitations. It can only be used when the serum samples are not haemolysed or contaminated, and conditions such...
as infection are absent. Erythrocytes have a high Zn content and in cases of Zn deficiency red cell fragility is increased (Bettger et al. 1978). Parasitaemia is prevalent in many developing countries, and its presence confounds the interpretation of serum Zn concentrations; during infection values are spuriously low because Zn is redistributed from the plasma to other tissues (Aggett, 1991; Filteau & Tomkins, 1994). Other important confounding factors which must be controlled when collecting blood samples for plasma Zn analysis include diurnal variation in circulating Zn level, fasting, meal consumption, the time interval between blood collection and separation of the plasma, and contamination of the blood sample from evacuated tubes with rubber stoppers and non-acid washed glassware (Gibson, 1989; Aggett, 1991; Wallock et al. 1993). In general, low plasma/serum Zn levels indicate deficiency or a redistribution of Zn, but normal levels do not necessarily preclude deficiency. For instance, in cases of chronic but mild Zn deficiency states, plasma concentrations are often normal (Gibson et al. 1989b; Ruz et al. 1991), making diagnosis difficult.

Alternative static biochemical indices of Zn status which have been investigated include the concentrations in hair, urine, leucocytes, neutrophils, platelets and saliva. Available evidence suggests that low concentrations in hair samples collected during infancy and childhood probably reflect chronic suboptimal Zn status when the confounding effects of severe protein–energy malnutrition and season are absent (Hambidge et al. 1972; Gibson et al. 1989b; Cavan et al. 1993a; Ferguson et al. 1993b). Clinical features of mild Zn deficiency in childhood, such as impairments in linear growth, appetite and taste acuity, have been associated with hair concentrations of less than 1.07 μmol/g (70 μg/g) (Hambidge et al. 1972; Krebs et al. 1984; Smit Vanderkooy & Gibson, 1987) in the summer, and less than 1.68 μmol/g (110 μg/g) in the winter (Gibson et al. 1989b; Cavan et al. 1993a). In some cases, the low hair concentrations have been related to poorly available dietary Zn (Smit Vanderkooy & Gibson, 1987; Ferguson et al. 1988; Gibson et al. 1991b; Cavan et al. 1993a).

Hair Zn cannot be used in cases of very severe malnutrition when the rate of growth of the hair shaft is often diminished. In such cases, hair Zn concentrations may be normal or even high (Erten et al. 1978; Bradfield & Hambidge, 1980). Standardized procedures must be used for sampling, washing, and analysing the hair samples (Hambidge, 1982). Supplementation trials must be undertaken over one year and all the subjects sampled at the same season of the year to minimize the confounding effects of seasonal variation (Gibson et al. 1989a).

Many investigators have failed to find any positive correlations between the Zn content of hair and serum/plasma Zn concentrations (Hambidge et al. 1972; Walravens et al. 1983, 1989; Gibson et al. 1989b). These findings are not unexpected. The Zn content of the hair shaft reflects the quantity of Zn available to the hair follicle over an earlier time interval. Positive correlations between hair and plasma Zn concentrations are only observed in chronic, severe deficiency states, in the absence of confounding factors.

Depletion of body Zn stores causes a reduction in urinary excretion, often before any detectable changes in serum/plasma Zn concentrations (Baer & King, 1984). Twenty-four hour urine collections are recommended because diurnal variation in urinary Zn excretion occurs, although casual urine samples can be used if Zn:creatinine ratios are determined (Zlotkin & Casselman, 1988). Several factors can affect urinary Zn concentrations, however, making interpretation of the results difficult. For example, despite the presence of suboptimal Zn status in sickle cell anaemia, hyperzincuria occurs. The absence of established interpretive criteria for urinary Zn levels further limits their use (Gibson, 1989).

The Zn contents of leucocytes or specific cellular types of leucocytes (e.g. neutrophils) have been used as an index of tissue Zn status; they are said to reflect soft tissue Zn (Jones
et al. 1981) and correlate with retinal dark adaptation. They also have a shorter half-life than erythrocytes and hence should detect changes in Zn status over a shorter time period. Results, however, have been equivocal (Jones et al. 1981; Meadows et al. 1981; Prasad & Cossack, 1982; Thompson, 1991; Ruz et al. 1992). Relatively large volumes of blood are required and isolation of the leucocytes and specific cellular types, as well as their subsequent analysis, is lengthy and technically difficult, limiting their use in some countries. For example, Milne et al. (1985) have emphasised that the Zn content of leucocytes is a function of the type of separation used; contamination with Zn from the anticoagulant, reagents, density gradient system, and/or from erythrocytes and platelets may occur. Changes in the relative proportions of leucocyte subsets with physiological state (e.g. pregnancy) and haematological disorders must also be taken into account in the interpretation of the results. Finally, comparison of results among different studies is difficult because no consensus exists as to how to express Zn concentrations in the cell types.

Biochemical functional tests measure changes in the activities of certain enzymes or blood components dependent on Zn. Zinc is a constituent of over 200 metallo-enzymes which vary in their responses to Zn deficiency depending on the tissue examined, their Zn affinity, and rate of turnover of the enzyme. Of the Zn metallo-enzymes, activity of serum alkaline phosphatase has been most widely used to assess Zn status; its response has been inconsistent. In general, its activity is reduced in severe (Rothbaum et al. 1982) but not in mild (Ruz et al. 1991) Zn deficiency states. No significant changes in activity have been reported in mild Zn depletion-repletion studies of adults (Ruz et al. 1991), or in most (Hambidge et al. 1972; Walravens & Hambidge, 1976; Walravens et al. 1983, 1989; Gibson et al. 1989b; Cavan et al. 1993b), but not all (Udomkesmalee et al. 1992) of the Zn supplementation studies in infants and children.

The specificity of alkaline phosphatase as an index of Zn status is also poor; its activity is influenced by many factors other than Zn status such as low food intake, type of protein consumed, magnesium or manganese deficiency, season, and in states of increased bone turnover (Chesters & Will, 1978; Koo et al. 1989). Measurements of alkaline phosphatase activity in neutrophils (Ruz et al. 1991), leucocytes (Schiliro et al. 1987), and red blood cell membranes (Ruz et al. 1992; Cavan et al. 1993b) have also been investigated as indices of Zn status; more studies are needed before any definite conclusions can be reached. To date, there is no universally accepted Zn dependent enzyme which can be used to assess mild Zn deficiency.

Levels of the Zn binding protein metallothionein have been investigated in serum, urine, or erythrocytes as indices of Zn status (Golden, 1989). Levels fall in Zn deficiency as a result of impaired synthesis. Specificity is poor; levels are also affected by Fe deficiency, diurnal rhythm, and acute infection. Metallothionein is said to be much less responsive to stress and infection in erythrocytes than in plasma (Grider et al. 1990), and hence may provide a useful index of Zn status.

Serum thymulin has also been assessed as a potential index of Zn status. Thymulin is a Zn metallopeptide which controls cell mediated immune function (Prasad et al. 1988); its activity falls in mild Zn deficiency. Plasma somatomedin-C, a peptide of low molecular weight which is regulated by growth hormone, nutrition, and insulin, is increased in response to increases in Zn concentration in plasma and tibia of rats. Nevertheless, more work is required to establish the sensitivity, specificity, and validity of erythrocyte metallothionein, serum thymulin and somatomedin-C as indices of Zn status.
PHYLOGICAL FUNCTIONAL INDICES OF ZINC STATUS

Physiological functions dependent on Zn, such as linear and ponderal growth, taste acuity, and immune competence, can also be used to assess Zn status. Such tests have greater biological significance than the biochemical tests because they measure the biological impact of Zn deficiency. Their specificity is low, and hence they must always be used in conjunction with biochemical indices.

Diminished taste acuity is a feature of mild Zn deficiency. Several methods for testing taste acuity have been used. In studies of Canadian (Gibson et al. 1989b) and Guatemalan (Cavan et al. 1993a) children, significant inverse relationships between recognition threshold for salt and hair Zn concentrations have been noted. These results suggest that impaired taste acuity can be used as a physiological functional test of suboptimal Zn nutruiure in some children, provided a biochemical index of Zn status is also used. The test is not suitable, however, for infants and children less than five years of age.

Some changes in body composition have also been observed after Zn supplementation in some cases of deficiency in children. Specifically, increases in arm circumference were reported in Gambian children (Bates et al. 1993), whereas in Zn supplemented Jamaican children recovering from severe malnutrition, accretion of lean tissue was greater. The latter was attributed to an increased efficiency of nutrients for tissue synthesis after Zn supplementation. By contrast, triceps skin folds increased in Guatemalan Zn supplemented children (Cavan et al. 1993b), probably due to an increase in energy intake concomitant with improved appetite.

From the discussion above, it is evident that diagnosis of Zn deficiency is hampered by the lack of a single, specific, and sensitive index of status. A large number of indices have been proposed, but many are fraught with problems that affect their use and interpretation, especially in mild Zn deficiency states. Hence, it is not surprising that the true magnitude of Zn deficiency in developing countries is not yet known.

ZINC DEFICIENCY THROUGHOUT THE LIFE CYCLE

INFANCY AND CHILDHOOD

Cases of severe Zn deficiency in infancy and childhood are now rare but mild deficiency in infancy and childhood is not uncommon. Growth failure is the most prominent clinical feature of mild Zn deficiency, although impairments in body composition, taste acuity, appetite, immune function, dark adaptation, and delays in secondary sexual maturation have also been described (Hambidge, 1989). Growth failure is also a characteristic feature of childhood growth patterns in many developing countries, which has until recently been attributed to deficits in energy and/or protein. Inadequate Zn intakes are likely to be an important contributing factor because diets low in protein tend to be low in Zn (Golden & Golden, 1981b), and Zn has such a critical role in protein synthesis, cell replication, and appetite control.

The first cases of human Zn deficiency were reported in the Middle East among adolescent male dwarfs in the 1960s (Prasad et al. 1963). The syndrome was characterized by impaired growth and delayed sexual maturation, which were shown to respond to Zn supplementation in later studies (Ronaghy et al. 1969, 1974).

Since these first reports, nutritional Zn deficiency has been reported in infants and/or children living in some industrialized (Hambidge et al. 1972; Walravens & Hambidge, 1976; Arcasoy et al. 1978; Buzina et al. 1980; Walravens et al. 1983, 1989, 1992; Smit Vanderkooy & Gibson, 1987; Gibson et al. 1989b), and developing (Golden &
### Table 3. Double-blind zinc supplementation studies in infants

<table>
<thead>
<tr>
<th>Country, no. of subjects, age of subjects, experimental treatment, reference</th>
<th>Mean plasma zinc levels, (μmol/l)</th>
<th>Growth effects and other responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA. 68 normal healthy full term male infants at birth studied for 6 months. Double-blind study. Formula with 1.8 mg Zn/l v. 5.8 mg Zn/l. Walravens &amp; Hambidge, 1976</td>
<td>Zinc suppl.</td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td>Start</td>
<td>End</td>
</tr>
<tr>
<td></td>
<td>11.9</td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td>Improved weight and length in males only.</td>
<td></td>
</tr>
<tr>
<td>France. 57 normal healthy infants 5-4 months old studied for 3 months. Double-blind placebo (32), 5 mg Zn/d (25). Walravens et al. 1992</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA. 50 failure to thrive, 8-27 months old studied for 6 months. Randomized double-blind trial pair-matched. 57 mg Zn/d as syrup (25) and placebo (25). Walravens et al. 1989</td>
<td>10.7</td>
<td>9.8</td>
</tr>
<tr>
<td>Chile. 32 marasmic infants, 7-8 months old, studied for 90 d. Randomized double-blind trial. 2 mg Zn/kg daily as solution (16). Placebo (16). Castillo-Duran et al. 1987</td>
<td>14.7</td>
<td>15.6</td>
</tr>
<tr>
<td>Chile. 39 severely malnourished infants studied for 105 d. Double-blind trial 1.9 mg Zn/kg daily in formula (19) v. 0.35 mg Zn/kg daily in formula (20). Schlesinger et al. 1992</td>
<td>19.4</td>
<td>18.6</td>
</tr>
<tr>
<td>Bangladesh. 60 severely malnourished infants 5-60 months old for 3 weeks. Rice based diet ad lib. and vitamins and minerals. 10 mg Zn/kg daily if &lt; 6 kg or 50 mg Zn/d for those &gt; 6 kg as ZnSO₄. Non-supplemented group (30). Khanum et al. 1988</td>
<td>8.2</td>
<td>18.5</td>
</tr>
<tr>
<td>Bangladesh. 65 children with AD 3-24 months old. 152 with PD 3-24 months old supplemented for 2 weeks. Followed for 2 and 3 months in a double-blind randomized study (placebo v. 15 mg Zn/kg daily). Roy et al. 1993</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chile. 80 SGA neonates 38-41 weeks gestational age studied from birth for 6 months. Double-blind randomized study with placebo (41), 3 mg Zn/d (39). Rodriguez et al. 1991</td>
<td>12.6</td>
<td>10.5</td>
</tr>
</tbody>
</table>

AD, acute diarrhoea; PD, persistent diarrhoea; SGA, small for gestational age.
Table 4. Double-blind zinc supplementation studies in children

<table>
<thead>
<tr>
<th>Country, date, number of subjects, age of subjects, experimental treatment, reference</th>
<th>Dietary zinc intake (mg)</th>
<th>Zinc suppl.</th>
<th>Control</th>
<th>Growth effect and other responses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Start</td>
<td>End</td>
<td></td>
</tr>
<tr>
<td>Egypt. 1965–6. 90 growth retarded school boys, 11–18 years old studied for 5.5 months. Randomized trial, placebo (30) and 14 mg Zn (30). Capsules given at school. Carter et al. 1969</td>
<td>14</td>
<td>10.7</td>
<td>19.2</td>
<td>11.7</td>
</tr>
<tr>
<td>Iran. 1967–8. 60 growth retarded school boys 12–18 years old studied for 17 months (5 months trial, 7 months rest, 5 months trial). Controlled trial. 1st 5 months placebo (20), 28 mg Zn (20), 67 mg Fe (20). 2nd 5 months placebo (20), micronutrients (20), micronutrients + 40 mg Zn (20). Capsules given at school. Ronaghy et al. 1969</td>
<td>12</td>
<td>17.2</td>
<td>14.7</td>
<td>11.6</td>
</tr>
<tr>
<td>Iran. 1969–71. 50 growth retarded school boys 13 years old studied for 17 months (5 months trial, 7 months rest, 5 months trial). Non-randomized trial placebo (10), micronutrients (20), micronutrients + 40 mg Zn (20). Capsules given at school. Ronaghy et al. 1974</td>
<td>12</td>
<td>8.2</td>
<td>10.2</td>
<td>10.5</td>
</tr>
<tr>
<td>USA, Colorado. 40 growth retarded, low Zn status children 2–6 years old studied for 1 year. Randomized pair-matched trial with placebo (20) and 10 mg Zn/d (20). Syrup given by parents at home. Walravens et al. 1983</td>
<td>46</td>
<td>10.7</td>
<td>10.8</td>
<td>11.3</td>
</tr>
<tr>
<td>Canada. 1986. 60 growth retarded boys 5–7 years old studied for 12 months. Randomized pair-matched trial with placebo (30) and 10 mg Zn/d (30). Fruit juice drink given by parents at home. Gibson et al. 1989</td>
<td>64</td>
<td>15.6</td>
<td>16.2</td>
<td>16.5</td>
</tr>
</tbody>
</table>
Thailand. 1989–90. 133 children 6–13 years old with suboptimal Zn and vitamin A nutriture for 6 months. Randomized pair-matched trial with placebo (35), 25 mg Zn/d (33), vit. A + Zn (32). Capsules taken on school days. Udomkesmalee et al. 1992

The Gambia. 1989–90. 109 apparently healthy children 1/2 to 3 years old for 15 months. Randomized group matched trial with placebo (54), and 70 mg Zn (55) as a drink twice a week at clinic. Bates et al. 1993


Chile. 1991. 46 short stature school children, 6–12 years old, consuming diets providing 50–60% of normal daily Zn intake. 12 month randomized study involving placebo v. 10 mg Zn/d. Castillo-Duran et al. 1987

Chile. 1993. 98 healthy preschool children studied for 14 months. Placebo v. 10 mg Zn/d. Ruz, 1992

No weight or height effect. Increase in serum alkaline phosphatase activity. Improved dark adaption. Improved conjunctiva integrity.

No weight or height effect. Increase in arm circumference. Less malaria. Improved intestinal permeability.

No weight or height effect. Increase in triceps skinfold. Smaller decrease in mid arm circumference. No increase in serum alkaline phosphatase.

No weight effect. Height effect in males only. No difference in plasma Zn.

Height effect in males. Trend in improved immune function and reduced giadiasis.
Golden, 1981a; Xue-Cun et al. 1985; Castillo-Duran et al. 1987; Khanum et al. 1988; Simmer et al. 1988; Udomkesmalee et al. 1990, 1992; Schlesinger et al. 1992; Bates et al. 1993; Cavan et al. 1993a, b; Roy et al. 1993; M. Ruz, 1993, pers. comm.; Smith et al. 1993) countries (Tables 3 & 4). In most of these studies, clinical signs of severe Zn deficiency were not apparent. Instead, mild Zn deficiency existed, characterized by reductions in linear and/or ponderal growth, and/or impairments in taste acuity, appetite, immune and intestinal function, and dark adaptation, some of which have responded positively to Zn supplementation in double-blind studies. Biochemical evidence of Zn deficiency has not been a consistent finding. This is not unexpected; physiological functional consequences (e.g. growth retardation) of mild Zn deficiency are often apparent before the Zn concentrations in plasma and/or tissues are significantly reduced (Gibson et al. 1989b; Ruz et al. 1991), emphasizing the importance of confirming mild Zn deficiency by a positive response to a supplement in double-blind studies.

PREGNANCY

Animal studies have clearly demonstrated the teratogenic effects of Zn deficiency (Hurley & Swenerton, 1966), but results of human studies have been inconsistent. In severe Zn deficiency in humans arising from acrodermatitis enteropathica, abortions and gross congenital malformations (e.g. anencephaly) have been reported (Hambidge et al. 1975). The existence of mild Zn deficiency during pregnancy and its effect on pregnancy outcome is less clear, in part because of difficulties in establishing the existence of marginal Zn status during pregnancy and/or inadequacies in the experimental designs. No double-blind Zn supplementation studies during pregnancy have been carried out in developing countries.

Serum Zn has been the most frequently used index of Zn status during pregnancy; it declines during pregnancy even in the presence of optimal maternal Zn nutriture (Swanson & King, 1987), attributed in part to expansion in plasma volume. Nevertheless, in women with inadequate Zn intakes, the decline in serum Zn during pregnancy may be abnormally large (Hambidge et al. 1983; Cherry et al. 1989).

Relationships between maternal plasma Zn and pregnancy outcome have been inconsistent, and have varied with both the stage of gestation and the outcome variable measured (Swanson & King, 1987). For example, plasma Zn correlated weakly with birth weight when sampled at mid pregnancy (McMichael et al. 1982), more strongly in early rather than in later pregnancy, i.e. third trimester (Neggars et al. 1990), or not at all (Arcasoy et al. 1978; Buzina et al. 1980; Hambidge et al. 1983; Campbell-Brown et al. 1985; Hunt et al. 1985; Tuttle et al. 1985; Mahomed et al. 1989). Plasma Zn has also been reported to correlate with pregnancy complications such as prolonged labour, hypertension, postpartum haemorrhage, spontaneous abortions, and/or congenital malformations by some (Jameson, 1976; Çavdar et al. 1980, 1991; Cherry et al. 1981; McMichael et al. 1982; Soltan & Jenkins, 1982; Hunt et al. 1985) but not all (Breskin et al. 1983; Mukherjee et al. 1984) investigators. In some double-blind Zn supplementation studies, significant reductions in pregnancy complications have been observed in the Zn treated compared to the placebo group (Hunt et al. 1984; Cherry et al. 1989; Jameson et al. 1990; Simmer et al. 1991) (Table 5), associated in some cases with alterations in prostaglandin metabolism (O'Dell et al. 1977).

Some relationships have also been reported between low maternal Zn concentrations in leucocytes and/or lymphocytes and intrauterine growth retardation (Meadows et al. 1981; Simmer & Thompson, 1985), low birth weight (Wells et al. 1987; Malhotra et al. 1990), and neural tube defects (Hinks et al. 1989). In two double-blind Zn supplementation studies
Table 5. Zinc supplementation studies in pregnant women

<table>
<thead>
<tr>
<th>Country, date, type of subjects, experimental treatment, reference</th>
<th>Dietary zinc intake (mg)</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK. 1985–6. 494 middle class women studied for last 4 months of pregnancy. Randomized double-blind trial with placebo (248) and 20 mg Zn/d (246). Capsules taken at home. Mahomed et al. 1989</td>
<td>9</td>
<td>No effect on birth weight. No difference in leucocyte Zn in supplemented and placebo group.</td>
</tr>
<tr>
<td>USA, New Orleans. 556 low income adolescent women studied for last 3 months of pregnancy. Randomized double-blind trial with placebo (288) and 30 mg Zn/d (268). Tablets taken at home. Cherry et al. 1989</td>
<td>?</td>
<td>No effect on birth weight. Reduced rates of prematurity and neonatal morbidity.</td>
</tr>
<tr>
<td>USA, Los Angeles. 1981–2. 138 Hispanic teenagers studied for last 4 months of pregnancy. Randomized double-blind trial with micronutrients (+20 mg Zn/d) and micronutrients (+20 mg Zn/d). Capsules taken at home. Hunt et al. 1985</td>
<td>9-8</td>
<td>No effect on birth weight.</td>
</tr>
<tr>
<td>USA, Los Angeles. 213 Hispanic low income women enrolled &lt; 27 week gestation age. Randomized double-blind trial with micronutrients (106) and micronutrients +20 mg Zn/d (107). Capsules taken at home. Hunt et al. 1984</td>
<td>9-3</td>
<td>No effect on birth weight. Reduced incidence of pregnancy induced hypertension.</td>
</tr>
<tr>
<td>UK. 56 pregnant females at risk of SGA infants. Studied last 15–25 weeks. Randomized double-blind trial with placebo (26) and 22.5 mg Zn/d (30). Simmer et al. 1991</td>
<td>?</td>
<td>Lower incidence of IUGR. Labour induced less often. C-section less often.</td>
</tr>
<tr>
<td>USA. 46 pregnant middle income females studied for 7–9 months. Not randomized double-blind study. Placebo (36) vs. 15 mg Zn/d (10). Tablet taken 2 h after dinner. Hambidge et al. 1983</td>
<td>11</td>
<td>No effect on birth weight. No other effects observed.</td>
</tr>
</tbody>
</table>

C-section, Caesarian section; IUGR, intra-uterine growth retardation; SGA, small for gestational age.

(Mahomed et al. 1989; Thauvin et al. 1992), however, no differences in leucocyte Zn concentrations between the two groups were observed.

Several adaptive mechanisms exist during pregnancy to help meet the increased demands for Zn, including an increase in absorption, a reduction in endogenous losses, redistribution of tissue Zn, and an efficient maternal–fetal transfer (Swanson & King, 1987). Although such adaptive mechanisms may be adequate to prevent Zn deficiency in women in developed countries, they may not be sufficient for pregnant women from developing countries, whose Zn status may be especially low because of frequent reproductive cycling, excessive losses of endogenous Zn, combined with diets low in readily available Zn. Unfortunately, however, investigations of the Zn status of pregnant women in developing countries are limited (Çavdar et al. 1980; Prema, 1980; Okonofua et al. 1989, 1990); none has involved double-blind Zn supplementation trials.

In view of the inconsistencies noted above, the precise nature of the association between Zn status and pregnancy outcome remains unclear. Existing evidence suggests that the prevalence of deficiency in women during pregnancy in developing countries is likely to be...
Table 6. Double-blind zinc supplementation studies in lactating women

<table>
<thead>
<tr>
<th>Country, no. of subjects, type of subjects, experimental treatment, reference</th>
<th>Dietary zinc intake (mg)</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil, Amazon region. 65 poor urban women studied for first 5 months of lactation. Randomized trial with placebo (28) and group consuming 15 mg Zn/d (37). Capsules taken at home. Shrimpton et al. 1983 and Shrimpton et al. 1985</td>
<td>23</td>
<td>No effect on milk Zn levels. Milk vitamin A levels increased. Less diarrhoea in infants.</td>
</tr>
<tr>
<td>USA, Colorado. 53 middle income lactating women, for varying durations up to 9 months. Controlled (8) trial with placebo (39) and group consuming 15 mg Zn/d (14). Tablets taken at home. Krebs et al. 1985</td>
<td>12.2</td>
<td>Decreased fall in milk Zn levels.</td>
</tr>
<tr>
<td>USA, Indiana. 49 middle income mothers studied during first 6 months of lactation. Controlled trial with groups consuming micronutrients (25) and micronutrients + 25 mg Zn (24). Different commercial supplements taken at home. Karra et al. 1986</td>
<td>11.2</td>
<td>Higher milk Zn levels.</td>
</tr>
<tr>
<td>USA, Maryland. 40 middle income women studied during the first 6 months of lactation. Randomized double-blind trial with groups consuming micronutrients (20) and micronutrients + 25 mg Zn/d (20). Tablets taken at home. Moser-Veillon &amp; Reynolds, 1990</td>
<td>12</td>
<td>No effect on milk Zn levels.</td>
</tr>
</tbody>
</table>

higher than that in developed countries, but large, well designed, double-blind Zn supplementation trials are required to confirm the existence of nutritional deficiency and its precise impact on pregnancy outcome.

**LACTATION**

Studies of maternal Zn status during lactation are limited (Table 6). Some have documented low plasma concentrations in the presence of normal concentrations in hair, urine (Jackson et al. 1988), and/or breast milk, even in poorly nourished lactating women with chronically inadequate intakes of dietary Zn (Kirsten et al. 1985; Karra et al. 1986; Simmer et al. 1990). Two Zn supplementation studies during lactation (Krebs et al. 1985; Shrimpton et al. 1985) documented a reduction in the abnormally steep decline in breast milk Zn content during late lactation, although the numbers of subjects in these studies were small. Furthermore, the incidence of diarrhoea in the infants decreased, and milk retinol content was maintained at a higher level throughout lactation in the Zn supplemented Amazonian women (Shrimpton et al. 1983, 1985).

By contrast, in a US study in Indiana (Karra et al. 1986) in which 25 mg Zn/d were given, Zn levels of breast milk apparently increased. Such increases were not observed by Moser-Veillon & Reynolds (1990), despite a comparable daily Zn supplement to US Maryland lactating women. The study of Karra et al. (1986), unlike the Maryland study (Moser-Veillon & Reynolds, 1990), was not a double-blind randomized trial.

Even in malnourished women from developing countries whose breast milk Zn concentrations are not compromised, their volume of breast milk may be reduced (Brown
et al. 1986), thus contributing to growth failure in early infancy. Traditional weaning foods used in many developing countries are often based on unrefined cereals and/or legumes, low in bioavailable Zn. If these weaning foods are not processed to reduce their phytic acid content, their use may further compromise infant growth, especially if they replace rather than complement breast milk (Walker, 1990). Strategies which can be used in developing countries to reduce the phytic acid content of traditional staple foods, including weaning foods, are outlined below.

NUTRITION INTERVENTION STRATEGIES TO PREVENT ZINC DEFICIENCY IN DEVELOPING COUNTRIES

Both short term and long term nutrition intervention strategies can be used to prevent Zn deficiency in developing countries: (1) supplementation; (2) fortification; and (3) dietary modification/diversification using traditional household techniques. For pregnant women, supplementation or fortification is appropriate because a relatively short term response is required to improve their Zn status before the end of pregnancy. Moreover, requirements for Zn during pregnancy, like Fe, cannot be met from dietary sources alone. Such approaches can also be used to provide several micronutrients simultaneously. They do, however, rely on a stable infrastructure and require financial support on a long standing economic basis if they are to be successful. All too often such programmes have been suspended for economic, political, and logistical reasons.

The third approach, dietary modification/diversification, involves changes in food selection patterns and/or traditional household methods for preparing and processing indigenous foods. It is a more economically feasible, culturally acceptable, and sustainable intervention for alleviating Zn deficiency in developing countries. Possible dietary changes to improve both the content and bioavailability of Zn include increasing the consumption of flesh foods, rich sources of readily available Zn, when economically feasible, and making modifications to food preparation and processing practices to reduce the level of the higher inositol phosphates in plant based staples. Higher inositol phosphates can be hydrolysed to lower inositol phosphates enzymically via fermentation and/or germination (Svanberg & Sandberg, 1988). Alternatively, in some cases non-enzymic hydrolysis of the higher inositol phosphates can be achieved by thermal processing, or soaking, provided the phytic acid is present as the soluble potassium salt (Reddy et al. 1989). The extent of the hydrolysis of the higher inositol phosphates can be monitored using the HPLC method for phytic acid analysis (Lehrfeld, 1989). The latter, unlike the AOAC method (Harland & Oberleas, 1986), differentiates the hexaphosphate and pentaphosphate from the lower inositol phosphates. Only the former inhibit the bioavailability of Zn (Tao et al. 1986; Lönnerdal et al. 1989).

To be successful, these dietary modifications/diversifications must be introduced using well designed educational and social marketing projects aimed to change attitudes and dietary behaviours. To enhance their effectiveness and sustainability, they should be integrated into ongoing national health and nutrition programmes in developing countries which emphasize the broader health consequences of micronutrient deficiencies. This approach has been highly successful in the Philippines for controlling vitamin A deficiency (Solon, 1986). Implementation of these dietary strategies could have far reaching consequences for both maternal and infant health in many developing countries, decreasing morbidity and complications in pregnancy, reducing mortality during childbirth, risk of prematurity and low birth weight, and enhancing growth and development in infancy and childhood.
REFERENCES


