Chapter 16
Zinc

Role of zinc in human metabolic processes

Zinc is present in all body tissues and fluids. The total body zinc content has been estimated to be 30 mmol (2 g). Skeletal muscle accounts for approximately 60 percent of the total body content and bone mass, with a zinc concentration of 1.5–3 μmol/g (100-200 μg/g), for approximately 30 percent. Zinc concentration of lean body mass is approximately 0.46 μmol/g (30 μg/g). Plasma zinc has a rapid turnover rate and it represents only about 0.1 percent of total body zinc content. This level appears to be under close homeostatic control. High concentrations of zinc are found in the choroid of the eye 4.2 μmol/g (274 μg/g) and in prostatic fluids 4.6-7.7 mmol/l (300-500 mg/l) (*1*).

Zinc is an essential component of a large number (>300) of enzymes participating in the synthesis and degradation of carbohydrates, lipids, proteins, and nucleic acids as well as in the metabolism of other micronutrients. Zinc stabilises the molecular structure of cellular components and membranes and contributes in this way to the maintenance of cell and organ integrity. Furthermore, zinc has an essential role in polynucleotide transcription and thus in the process of genetic expression. Its involvement in such fundamental activities probably accounts for the essentiality of zinc for all life forms.

Zinc plays a central role in the immune system, affecting a number of aspects of cellular and Humoral immunity (*2*). The role of zinc in immunity was reviewed extensively by Shanglar *et al*. (*2*).

The clinical features of severe zinc deficiency in humans are growth retardation, delayed sexual and bone maturation, skin lesions, diarrhoea, alopecia, impaired appetite, increased susceptibility to infections mediated via defects in the immune system, and the appearance of behavioural changes (*1*). The effects of marginal or mild zinc deficiency are less clear. A reduced growth rate and impairments of immune defence are so far the only clearly demonstrated signs of mild zinc deficiency in humans. Other effects, such as impaired taste and wound healing, which have been claimed to result from a low zinc intake, are less consistently observed.

Zinc metabolism and homeostasis

Zinc absorption is concentration dependent and occurs throughout the small intestine. Under normal physiologic conditions, transport processes of uptake are not saturated. Zinc administered in aqueous solutions to fasting subjects is absorbed efficiently (60–70 percent), whereas absorption from solid diets is less efficient and varies depending on zinc content and diet composition (*3*).

Zinc is lost from the body through the kidneys, skin, and intestine. The endogenous intestinal losses can vary from 7 μmol/day (0.5 mg/day) to more than 45 μmol/day (3 mg/day), depending on zinc intake (*4*). Urinary and skin losses are of the order of 7-10 μmol/day (0.5–0.7 mg/day) each and depend less on normal variations in zinc intake (*4*). Starvation and muscle catabolism increase zinc losses in urine. Strenuous exercise and elevated ambient temperatures could lead to losses by perspiration.

The body has no zinc stores in the conventional sense. In conditions of bone resorption and tissue catabolism, zinc is released and may be re-utilised to some extent. Human experimental studies with low-zinc diets 2.6–3.6 mg/day (40-55 µmol/day) have shown that circulating zinc levels and activities of zinc-containing enzymes can be maintained within normal range over several months (*5*, *6*), which highlights the efficiency of the zinc homeostasis mechanism. Controlled depletion-repletion studies in humans have shown that changes in the endogenous excretion of zinc through the kidneys, intestine, and skin and changes in absorptive efficiency are how body zinc content is maintained (*7-10*). The underlying mechanisms are poorly understood.

Sensitive indexes for assessing zinc status are unknown at present. Static indexes, such as zinc concentration in plasma, blood cells, and hair, and urinary zinc excretion are decreased in severe zinc deficiency. A number of conditions that are unrelated to zinc status can affect all these indexes, especially zinc plasma levels. Infection, stress situations such as fever, food intake, and pregnancy lower plasma zinc concentrations whereas, for example, long-term fasting increases it (*11*). However, on a population basis, reduced plasma zinc concentrations seem to be a marker for zinc-responsive growth reductions (*12*, *13*). Experimental zinc depletion studies suggest that changes in immune response occur before reductions in plasma zinc concentrations are apparent (*14*). So far, it has not been possible to identify zinc-dependent enzymes which could serve as early markers for zinc status.

A number of functional indexes of zinc status have been suggested, for example, wound healing, taste acuity, and dark adaptation (*11*). Changes in these functions are, however, not specific to zinc and these indexes have so far not been proven useful for identifying marginal zinc deficiency in humans.

The introduction of stable isotope techniques in zinc research (*15*) has created possibilities for evaluating the relationship between diet and zinc status and is likely to lead to a better understanding of the mechanisms underlying the homeostatic regulations of zinc. Estimations of turnover rates of administered isotopes in plasma or urine have revealed the existence of a relatively small rapidly exchangeable body pool of zinc of about 1.5-3 mmol (100-200 mg) (*16-19*). The size of the pool seems to be correlated to habitual dietary intake and it is reduced in controlled depletion studies (*18*). The exchangeable zinc pool was also found to be correlated to endogenous faecal excretion of zinc (*19*) and to total daily absorption of zinc. These data suggest that the size of the exchangeable pool depends on recently absorbed zinc and that a larger exchangeable pool results in larger endogenous excretion. Changes in endogenous intestinal excretion of zinc seem to be more important than changes in absorptive efficiency for maintenance of zinc homeostasis (*19*).

Dietary sources and availability of zinc

Lean red meat, whole-grain cereals, pulses, and legumes provide the highest concentrations of zinc 25-50 mg/kg (380-760 µmol/kg) raw weight. Processed cereals with low extraction rates, polished rice, and lean meat or meat with high fat content have a moderate zinc content 10-25 mg/kg (150-380 µmol/kg). Fish, roots and tubers, green leafy vegetables, and fruits are only modest sources of zinc <10 mg/kg (<150 µmol/kg) (*20*). Separated fats and oils, sugar, and alcohol have a very low zinc content.

The utilisation of zinc depends on the overall composition of the diet. Experimental studies have identified a number of dietary factors as potential promoters or antagonists of zinc absorption (*21*). Soluble low-molecular-weight organic substances, such as amino and hydroxy acids, facilitate zinc absorption. In contrast, organic compounds forming stable and poorly soluble complexes with zinc can impair absorption. In addition, competitive interactions between zinc and other ions with similar physicochemical properties can affect the uptake and intestinal absorption of zinc. The risk for competitive interactions seems mainly to be related to high doses in the form of supplements or in aqueous solutions. However, at levels present in food and at realistic fortification levels, zinc absorption appears not to be affected, for example, by iron and copper (*21*).

Isotope studies with human subjects have identified two factors which together with the total zinc content of the diet are major determinants of absorption and utilisation of dietary zinc. The first is the content of inositol hexaphosphate (phytate) and the second is the level and source of dietary protein. Phytates are present in whole-grain cereals and legumes and in smaller amounts in other vegetables. They have a strong potential for binding divalent cations and their depressive effect on zinc absorption has been demonstrated in humans (*21)*. The molar ratio between phytates and zinc in meals or diets is a useful indicator of the effect of phytates in depressing zinc absorption. At molar ratios above the range of 6–10, zinc absorption starts to decline; at ratios above 15 absorption is typically less than 15 percent (*20*). The effect of phytate is, however, modified by the source and amount of dietary proteins consumed. Animal proteins improve zinc absorption from a phytate-containing diet. Zinc absorption from some legume-based diets is comparable with that from animal-protein-based diets despite a higher phytate content in the former. High dietary calcium potentiated the antagonistic effects of phytates on zinc absorption in experimental studies. The results from human studies are less consistent and any effects seem to depend on the source of calcium and the composition of the diet (*22*).

Some examples of recently published absorption studies illustrate the effect of zinc content and diet composition on fractional zinc absorption (***Table 53***) (*19, 23- 25*). The results from the total diet studies, where all main meals of a day's intake have been extrinsically labelled, show a remarkable consistency in fractional absorption despite relatively large variations in meal composition and zinc content. Thus, approximately twice as much zinc was absorbed from a non-vegetarian or high-meat diet (*24*, *25*) than from a diet in rural China based on rice and wheat flour (*20*). Data are lacking on zinc absorption from typical diets of developing countries, which usually have a high phytate content.

The availability of zinc from the diet can be improved by reductions in the phytate content and inclusion of animal protein sources. Lower extraction rates of cereal grains will result in lower phytate content but at the same time the zinc content is reduced, so that the net effect on zinc supply is limited. The phytate content can be reduced by activating the phytase present in most phytate-containing foods or through the addition of microbial or fungal phytases. Phytases hydrolyse the phytate to lower inositol phosphates, resulting in an improved zinc absorption (*26*, *27*). The activity of phytases in tropical cereals such as maize and sorghum is lower than that in wheat and rye (*28*). Germination of cereals and legumes increases phytase activity and addition of some germinated flour to ungerminated maize or sorghum followed by soaking at ambient temperature for 12–24 hours can reduce the phytate content substantially (*28*). Additional reduction can be achieved by the fermentation of porridge for weaning foods or doughs for bread making. Commercially available phytase preparations could also be used but may not be economically accessible in many populations.

Populations at risk for zinc deficiency

The central role of zinc in cell division, protein synthesis, and growth makes infants, children, adolescents, and pregnant women especially at risk for an inadequate zinc intake. Zinc-responsive stunting has been identified in several studies (*29*), and a more rapid body weight gain in malnourished children supplemented with zinc was reported. Other studies have failed to show a growth-promoting effect of zinc supplementation (*13*). A recent meta-analysis of 25 intervention trials comprising 1834 children under 13 years of age, with a mean duration of approximately 7 months and a mean dose of zinc of 14 mg/day (214 μmol/day), showed a small but significant positive effect of zinc supplementation on height and weight increases (*13*). The initial presence of stunting was significantly associated with an effect of zinc supplementation on height, whereas initial low plasma zinc concentrations were associated with a more pronounced effect on weight gain.

Results from zinc supplementation studies suggest that a low zinc status in children not only affects growth but is also associated with an increased risk of severe infectious diseases (*30*). Episodes of acute diarrhoea with shorter duration and less severity and reductions in incidence of diarrhoea in zinc-supplemented groups have been reported. Other studies indicate that the incidence of acute lower respiratory tract infections and malaria may also be reduced by zinc supplementation. Prevention of sub-optimal zinc status and zinc deficiency in children by an increased intake and availability of zinc could consequently have a significant effect on child health in developing countries.

The role of maternal zinc status on pregnancy outcome is still unclear. Positive as well as negative associations between plasma zinc concentration and foetal growth or labour and delivery complications have been reported (*31*). Results of zinc supplementation studies also remain inconclusive (*31*). Interpretation of plasma zinc concentrations in pregnancy is complicated by the effect of hemodilution, and low plasma zinc levels may reflect other metabolic disturbances (*11*). Zinc supplementation studies of pregnant women have been performed mainly in relatively well-nourished populations, which may be one of the reasons for the mixed results (*31*). A recent study in low-income American women with plasma zinc concentrations below the mean at enrolment in prenatal care showed that a zinc intake of 25 mg/day resulted in greater infant birth weights and head circumferences and a reduction in very low birth weights among non-obese women compared with the placebo group (*12*).

Table 53

Examples of fractional zinc absorption from total diets measured by isotope techniques

Subject characteristics *(ref.)*	**Diet/meal characteristics**	**Isotope technique**	**Zinc content μmol (mg)**	**Phytate-zinc molar ratio**	**Zinc absorption, %(x±SD)[a]**
Young adults (n=8) *(22)*	High-fibre diet	Radioisotopes	163 (10.7)	7	27±6
Young women (n=10) *(19)*	Habitual diet	Stable isotopes	124 (8.1)	10	34±9
Women (20-42years) (n=21) *(24)*	Lacto-ovo vegetarian	Radioisotopes	139 (9.1)	14	26 [b]
	Non-vegetarian	Radioisotopes	169 (11.1)	5	33 [b]
Women (20-42years) (n=21) *(24)*	Low meat	Radioisotopes	102 (6.7)	—	30 [c]
Postmenopausal women (n-14) *(25)*	High meat	Radioisotopes	198 (13.0)	—	28 [c]

[a] SD, standard deviation.
[b] Pooled SD=5.[c] Pooled SD=4.6.
Source: Adapted from FAO/WHO Trace Mineral Report(*32*)

Zinc requirements

The lack of specific and sensitive indexes for zinc status limits the possibilities for evaluating zinc requirements from epidemiologic observations. In the FAO/IAEA/WHO 1996 report (*32*), zinc requirements were estimated by using the factorial technique (i.e., by adding the requirements for tissue growth, maintenance, metabolism, and endogenous losses). Experimental zinc repletion studies with low zinc intakes have clearly shown that the body has a pronounced ability to adapt to different levels of zinc intakes by changing the endogenous zinc losses through the kidneys, intestine, and skin (*5-9,33*). The normative requirement for absorbed zinc was defined as the obligatory loss during the early phase of zinc depletion before adaptive reductions in excretion take place and was set at 1.4 mg/day for men and 1.0 mg/day for women. To estimate the normative maintenance requirements for other age groups, the respective basal metabolic rates were used for extrapolation. In growing individuals the rate of accretion and zinc content of newly formed tissues were used to obtain the data required for tissue growth. Similarly, the retention of zinc during pregnancy and the zinc concentration in milk at different stages of lactation were used to estimate the physiologic requirements in pregnancy and lactation (*32*).

The translation of these estimates of absorbed zinc to requirements for dietary zinc involves several considerations. First, the nature of the diet (i.e., its content of promoters and inhibitors of zinc absorption) determines the fraction of the dietary zinc that is potentially absorbable. Second, the efficiency of absorption of potentially available zinc is inversely related to the content of zinc in the diet. The review of available data from experimental zinc absorption studies of single meals or total diets resulted in a division of diets into three categories – high, moderate, and low zinc bio-availability – as detailed in ***Table 54*** (*32*). It was then discovered that the relationship between efficiency of absorption and zinc content differed for these diets (*32*). Algorithms were developed (*32*) and applied to the estimates of requirements for absorbed zinc to achieve a set of figures for the average individual dietary zinc requirements (***Table 55***). The fractional absorption figures applied for the three diet categories were 50 percent, 30 percent, and 15 percent, respectively. From these estimates and from the evaluation of data from dietary intake studies, mean population intakes were identified which were deemed sufficient to ensure a low prevalence of individuals at risk of inadequate zinc intake (*32*).

Infants, children, and adolescents

Endogenous losses of zinc in human-milk-fed infants were assumed to be 20 μg/kg/day (0.31μmol/kg/day) whereas 40 μg/kg/day (0.6 μmol/kg/day) was assumed for infants fed formula or weaning foods (*32*). For other age groups an average loss of 0.002 μmol/basal kJ (0.57 μg/basal kcal) was derived from the estimates in adults. Estimated zinc increases for infant growth were set at 120 and 140 μg/kg/day (1.83–2.14 μmol/kg/day) for female and male infants, respectively, for the first 3 months (*32*). These values decrease to 33 μg/kg/day (0.50 μmol/kg/day) for ages 6–12 months. For ages 1–10 years the requirements for growth were based on the assumption that new tissue contains 30 μg/g (0.46 μmol zinc/g) (*32*). For adolescent growth, a zinc content of 23 μg/g (0.35 μmol/g) increase in body weight was assumed. Pubertal growth spurts increase physiologic zinc requirements substantially. Growth of adolescent males corresponds to an increase in body zinc requirement of about 0.5 mg/day (7.6 μmol/day) (*32*).

Pregnancy

The total amount of zinc retained during pregnancy has been estimated to be 1.5 mmol (100 mg) (*34).* During the third trimester the physiologic requirement of zinc is approximately twice as high as that in women who are not pregnant (*32*).

Lactation

Zinc concentrations in human milk are high in early lactation, 2-3 mg/l (31-46 µmol/l) in the first month, and fall to 0.9 mg/l (14 µmol/l) after 3 months (*35*). From data on maternal milk volume and zinc content, it was estimated that the daily output of zinc in milk during the first 3 months of lactation could amount to 1.4 mg/day (21.4 µmol/l), which would theoretically triple the physiologic zinc requirements in lactating women compared with non-lactating, non-pregnant women. In setting the estimated requirements for early lactation it was assumed that part of this requirement was covered by postnatal involution of the uterus and from skeletal resorption (*32*).

Elderly

Requirements for the elderly are estimated to be the same as those for other adults. A lower absorptive efficiency has been reported in the elderly, which could justify a higher dietary requirement. On the other hand, endogenous losses seem to be lower in the elderly. Because of the suggested role of zinc in infectious diseases, an optimal zinc status in the elderly could have a significant public health effect and is an area of zinc metabolism requiring further research.

Inter-individual variations in zinc requirements and recommended nutrient intakes

The studies (*6-10*) used to estimate the average physiologic requirements with the factorial technique have considered a relatively small number of subjects and do not allow any estimate of inter-individual variations in obligatory losses of zinc at different intakes. Because zinc requirements are related to tissue turnover rate and growth, it is reasonable to assume that variations in physiologic zinc requirements are of the same magnitude as variations in protein requirements (*36*) and that the same figure (12.5 percent) for the inter-individual coefficient of variation (CV) could be adopted. However, the estimates of dietary zinc requirements involve an estimate of absorption. Consequently, variations in absorptive efficiency, not relevant in relation to estimates of protein requirements, may have to be taken into account in the estimates of the total inter-individual variation in zinc requirements. Systematic studies of the inter-individual variations in zinc absorption under different conditions are few. In small groups of healthy well-nourished subjects, the reported variations in zinc absorption from a defined meal or diet are of the order of 20–40 percent and seem to be independent of age, sex, or diet characteristics. How much these variations, besides being attributable to methodologic imprecision, reflect variations in physiologic requirement, effects of preceding zinc intake, *etc*. is not known. From the available data from zinc absorption studies (*19, 20, 23-27*) it is tentatively suggested that the variation in dietary zinc requirements, which covers variation in requirement for absorbed zinc (i.e., variations in metabolism and turnover rate of zinc) and variation in absorptive efficiency, corresponds to a CV of 25 percent. The recommended nutrient intakes derived from the estimates of average individual dietary requirements (***Table 55***) with the addition of 50 percent (2 standard deviations) are given in ***Table 56***.

Table 54

Criteria for categorising diets according to the potential availability of their zinc

Nominal category	Principal dietary characteristics
High availability	Refined diets low in cereal fibre, low in phytic acid content, and with phytate-zinc (molar) ratio <5; adequate protein content principally from non-vegetable sources, such as meats, fish. Includes semisynthetic formula diets based on animal protein.
Moderate availability	Mixed diets containing animal or fish protein. Lacto-ovo, ovovegetarian, or vegan diets not based primarily on unrefined cereal grains or high-extraction-rate flours. Phytate-zinc molar ration of total diet within the range 5–15 or not exceeding 10 if more than 50% of the energy intake is accounted for by unfermented, unrefined cereal grains and flours whereas the diet is fortified with inorganic calcium salts (>1 g Ca^{2+}/ day). Availability of zinc improves when the diet includes animal or protein sources or milks.
Low availability	Diets high in unrefined, unfermented, and ungerminated cereal grain,[a] especially when fortified with inorganic calcium salts and when intake of animal protein is negligible. Phytate-zinc molar ration of total diet exceeds 15.[b] High-phytate soya-protein products constitute the primary protein source. Diets in which, singly or collectively, approximately 50% of the energy intake is accounted for by the following high-phytate foods: high-extraction-rate (90% +) wheat, rice, maize, grains and flours, oatmeal, and millet; chapatti flours and *tanok*; and sorghum, cowpeas, pigeon peas, grams, kidney beans, blackeye beans, and groundnut flours. High intakes of inorganic calcium salts (>1 g Ca^{2+}/ day), either as supplements or as adventitious contaminants (e.g., from calcareous geophagia), potentiate the inhibitory effects; low intakes of animal protein exacerbate these effects.

[a]Germination of such grains or fermentation (e.g., leavening) of many flours can reduce antagonistic potency; the diet should then be classified as moderate availability.

[b]Vegetable diets with phytate-zinc ratios exceeding 30 are not unknown; for such diets, an assumption of 10 percent availability of zinc or less may be justified, especially if the intake of protein is low, calcium salts is excessive, or both (e.g., calcium salts providing >1.5 g Ca^{2+}/day).

Table 55

Average individual normative requirements for zinc (μg/kg body weight/day) from diets differing in zinc bio-availability[a]

Age range years	High bio-availability[b]	Moderate bio-availability[c] μg/kg body weight/day	Low bio-availability[d]
Infants and Children			
Females, 0–0.25	175[e]	457[f]	1067[g]
Males, 0–0.25	200[e]	514[f]	1200[g]
0.25–0.5	79[e]	204[f]	477[g]
0.5–1	66[e]	—	—
0.5–1	186	311	621
1–3	138	230	459
3-6	114	190	380
6-10	90	149	299
Adolescents			
Females, 10–12	68	113	227
Males, 10–12	80	133	267
Females, 12–15	64	107	215
Males, 12–15	76	126	253
Females, 15–18	56	93	187
Males, 15–18	61	102	205
Adults			
Females, 18–60+	36	59	119
Males, 18–60+	43	72	144

Source: Adapted from FAO/IAEA/WHO (*32*).
[a] For information on diets, see ***Table 54***
[b] Assumed bio-availability of dietary zinc 50 percent.
[c] Assumed bio-availability of dietary zinc 30 percent.
[d] Assumed bio-availability of dietary zinc 15 percent.
[e] Applicable exclusively to infants fed maternal milk alone for which the bio-availability of zinc is with no allowance for storage.
[f] Applicable to infants partly human-milk-fed or fed whey-adjusted cow milk formula or milk plus low-phytate solids. No allowance for storage.
[g] Applicable to infants receiving phytate-rich vegetable-protein-based infant formula with or without whole-grain cereals. No allowance for storage.

Upper limits of zinc intake

Only a few occurrences of acute zinc poisoning have been reported. The toxicity signs are nausea, vomiting, diarrhoea, fever, and lethargy and have been observed after ingestion of 4-8 g (60-120 mmol) zinc. Long-term zinc intakes higher than the requirements could, however, interact with the metabolism of other trace elements. Copper seems to be especially sensitive to high zinc doses. A zinc intake of 50 mg/day (760 μmol) affects copper status indexes, such as CuZn-superoxide dismutase in erythrocytes (*37, 38*). Low copper and ceruloplasmin levels and anaemia have been observed after higher zinc intakes 450-660 mg/day (6.9-10 mmol/day) (*39, 40*). Changes in serum lipid pattern and in immune response have also been observed in zinc supplementation studies (*41, 42*). Because copper also has a central role in immune defence, these observations call for caution before large-scale zinc supplementation programmes are undertaken. Any positive effects of zinc supplementation on growth or infectious diseases could be disguised or counterbalanced by negative effects on copper-related functions.

The upper level of zinc intake for an adult man is set at 45 mg/day (690 μmol/day) and extrapolated to other groups in relation to basal metabolic rate. For children this extrapolation means an upper limit of intake of 23–28 mg/day (350–430 μmol/day), which is close to what has been used in some of the zinc supplementation studies. Except for excessive intakes of some types of seafood, such intakes are unlikely to be attained with most diets. Adventitious zinc in water from contaminated wells and from galvanized cooking utensils could also lead to high zinc intakes.

Table 56

Recommended nutrient intakes (RNIs) for dietary zinc (mg/day) to meet the normative storage requirements from diets differing in zinc bio-availability[a]

Age group	Assumed body weight, kg	High bio-availability	Moderate bio-availability	Low bio-availability
Infants and children				
0–6 months	6	1.1[b]	2.8[c]	6.6[d]
7–12 months	9	0.8[b]	–	–
7–12 months	9	2.5[e]	4.1	8.4
1–3 years	12	2.4	4.1	8.3
4–6 years	17	2.9	4.8	9.6
7–9 years	25	3.3	5.6	11.2
Adolescents				
Females, 10–18 years,	47	4.3	7.2	14.4
Males, 10–18 years	49	5.1	8.6	17.1
Adults				
Females, 19– 65 years	55	3.0	4.9	9.8
Males, 19–65 years	65	4.2	7.0	14.0
Females, 65+ years	55	3.0	4.9	9.8
Males, 65+ years	65	4.2	7.0	14.0
Pregnant Women				
First trimester	–	3.4	5.5	11.0
Second trimester	–	4.2	7.0	14.0
Third trimester	–	6.0	10.0	20.0
Lactating women				
0–3 months	–	5.8	9.5	19.0
3–6 months	–	5.3	8.8	17.5
6–12 months	–	4.3	7.2	14.4

[a]For information on diets, see ***Table 54***. Unless otherwise specified, the intra-individual variation of zinc requirements is assumed to be 25 percent. Weight data interpolated from FAO/WHO, 1988 (*36*).

[b]Human-milk-fed infants receiving maternal milk only; assumed coefficient of variation (CV) 12.5 percent; assumed availability 80 percent.

[c]Formula-fed infants: moderate bio-availability for whey-adjusted milk formula and for infants partly human-milk-fed or given low-phytate feeds supplemented with other liquid milks; assumed CV 12.5 percent.

[d]Formula-fed infants; low bio-availability applicable to phytate-rich vegetable-protein-based formula with or without whole-grain cereals; CV 12.5 percent.

[e]Not applicable to infants consuming human milk only.

Adequacy of zinc intakes in relation to requirement estimates

The risk for inadequate zinc intakes in children has been evaluated by using the suggested estimates of zinc requirements (*32*) and by using data available on food composition and dietary intake in different parts of the world (*43*). For this assessment it was assumed that the distribution of zinc requirements is Gaussian with a CV of 15 percent and that the correlation between intake and requirement is very low. Zinc absorption from diets in Malawi, Kenya, Mexico, and Guatemala was estimated to be 15 percent based on the high phytate-zinc molar ratio (*37-42*) in these diets, whereas an absorption of 30 percent was assumed for diets in Ghana, Guatemala, Egypt, and Papua New Guinea. Fermented maize and cassava products (*kenkey*, *banku*, and *gari*) in Ghana, yeast leavened wheat-based bread in Egypt, and the use of sago with a low phytate content as the staple in the New Guinean diets were assumed to result in a lower phytate-zinc molar ratio and a better availability. With this approach 68–94 percent of the children were estimated to be at risk for zinc deficiency in these populations, with the exception of Egypt where the estimate was 36 percent (*43*). The average daily zinc intakes of these children were 3.7-6.9 mg (56-105 µmol). Most of the zinc supplementation studies have not provided dietary intake data, which could be used to identify the zinc intake critical for growth effects. In a recent study in Chile, positive effects on height gain in boys after 14 months of zinc supplementation was noted (*44*). The intake in the placebo group at the start was 6.3 ± 1.3 mg/day (96 ± 20 µmol/day) (n=49). Because only 15 percent of the zinc intake of the Chilean children was derived from flesh foods, availability was assumed to be relatively low.

Krebs et al (*45*) observed no effect of zinc supplementation on human-milk zinc content or on maternal status of a group of lactating women and judged their intake sufficient to maintain adequate zinc status through 7 months or more of lactation. The mean zinc intake of the non-supplemented women was 13.0 ± 3.4 mg/day (199 ± 52 µmol/day).

The efficient homeostatic mechanisms for maintaining body zinc content at low intakes, which formed the basis for the estimates of physiologic requirements in the FAO/IAEA/WHO 1996 report (*32*), as well as the presumed negative impact of a high-phytate diet on zinc status, were confirmed in recent experimental studies (*10, 44, 46, 47*). Reductions in urinary and faecal losses maintained normal plasma zinc concentrations over 5 weeks in 11 men with intakes of 2.45 mg zinc/day (37 µmol/day) or higher in a diet with a presumably high availability (*10*). In a similar repletion-depletion study with 15 men, an intake of 4 mg/day (61 µmol/day) from a diet with a molar phytate-zinc ratio of 58 for 7 weeks resulted in a reduction of urinary zinc excretion from 0.52 ± 0.18 to 0.28 ± 0.15 mg/day (7.9 ± 2.8 µmol/day to 4.3 ± 2.3 µmol/day) (*46*). A significant reduction of plasma zinc concentrations and changes in cellular immune response were observed. Effects on immunity were also observed when a zinc-restricted diet with a high phytate content (molar ratio approximately 20) was consumed by five young male volunteers for 20–24 weeks (*14*). Sub-optimal zinc status has also been documented in pregnant women consuming diets with high phytate-zinc ratios (>17) (*47*). Frequent reproductive cycling and high malaria prevalence seemed to contribute to the impairment of zinc status.

Conclusion

In conclusion, the approach used for derivation of average individual requirements of zinc used in the FAO/IAEA/WHO 1996 report (32) and the resulting estimates still seem valid and useful for assessment of the adequacy of zinc intakes in population groups and for planning diets for defined population groups.

Future research

As already indicated in the FAO/IAEA/WHO 1996 report (*32*), there is an urgent need to characterise the early functional effects of zinc deficiency and to define their relation to pathologic changes. This knowledge is especially needed for understanding the role of zinc deficiency in the aetiology of stunting and impaired immunocompetence.

For a better understanding of the relationship between diet and zinc supply, there is a need for further research to carefully evaluate the availability of zinc from diets typical of developing countries. The research should include an assessment of the effect of availability of adopting realistic and culturally accepted food preparation practises such as fermentation, germination, soaking, and inclusion of inexpensive and available animal protein sources in plant-food-based diets.

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