26. Zinc

Physiology

Zinc is ubiquitous in the body. It has essential structural, regulatory or catalytic roles in many enzymes [1,2]; additionally it maintains the configuration of a number of non-enzymic proteins such as pre-secretory granules of insulin, some mammalian gene transcription proteins [3], and thymulin; it facilitates hormone and receptor binding at membrane and nuclear levels, and it may maintain integrity of biomembranes. Consequently zinc participates in gene expression and in the mechanisms and control of major metabolic pathways involving proteins, carbohydrates, nucleic acids and lipids.

An adult human contains about 2 g zinc of which 60 % and 30 % are in skeletal muscle and bone respectively, and 4-6 % is present in skin [2,4]. Zinc turnover in these tissues is slow and these depots do not provide a reliable source of zinc at times of deprivation. Since zinc is essential for the synthesis of lean tissue, it is whilst this is occurring that it may become a limiting nutrient. Although some zinc may be available in short term zinc deprivation from a mobile hepatic pool it is generally assumed that the body has no specific zinc reserve and is dependent on a regular dietary supply of the element .

Zinc is absorbed throughout the intestine. Proximal intestinal absorption is efficient, but since it has a large enteropancreatic circulation, net intestinal absorption of the metal is achieved by the distal small intestine. Relatively small amounts of zinc are lost in the urine. Homoeostasis at low and customary intakes is achieved by adjustments in net intestinal absorption and to a lesser extent by renal conservation [4,5]. With inappropriately high zinc intakes the systemic burden of the element is limited by its sequestration in the enterocyte by a cysteine-rich protein, metallothionein [2,4]. The amount of zinc lost in desquamated skin and shed hair and in sweat varies with preceding intakes.

Deficiency and excess

The classic features of severe zinc deficiency comprise the tetrad of neuropsychiatric disturbances, acrodermatitis and alopecia, diarrhoea, and increased susceptibility to infections as a manifestation of defective immune mechanisms (in particular cell-

mediated immunity). These features by and large represent the dependence on zinc of tissues with a high turnover [2,6]. However, there is currently an increasing interest in the occurrence in some children in Western communities, as well as in the Middle East, of a mild zinc deficiency syndrome manifest as zinc-responsive growth retardation [7,8].

Gross acute zinc toxicity has been described following the drinking of water which has been stored in galvanised containers or the use of such water for renal dialysis. Symptoms include nausea, vomiting, fever and are apparent after acute ingestion of 2 g or more of the element [2]. Of more general concern are the effects of supra-physiological intakes of zinc. Prolonged intakes of 75-300 mg/d have been associated with impaired copper utilisation, producing features such as microcytic anaemia and neutropenia, but even short term intakes of about 50 mg zinc daily interfere with the metabolism of both iron and copper [9]. It is not known if long-term adaptation of the metabolism of these metals would compensate for such interactions with zinc, however it would be unwise to exceed a daily zinc intake of 30 mg in adults.

Requirements

Adults

The assessment of zinc requirements in adults has been based on factorial analyses using measurements of basal losses during periods of extended deprivation, the turnover of radio-labelled endogenous zinc pools, and inference from observations in patients receiving total parenteral nutrition. None is ideal but all indicate that systemic supplies of 2-3 mg/d are adequate to avoid disturbed metabolism of other nutrients, and to support optimum nitrogen and carbohydrate metabolism.

In studies of human volunteers adapted to very low daily intakes of zinc (0.2-0.3 mg/d), faecal and urinary loss of the element falls to 1.4 and 0.9 mg/d in men and women respectively; it is probable that integumental (principally dermal) loss would fall similarly [10]. Allowing for losses of zinc in semen and menstruation, it has been estimated that basal losses are around 2.2 and 1.63 mg/d in men and women respectively [11]. Absorptive efficiency varies with intake [5,10]; at the levels being considered here, a value of 30% can be assumed, giving Average Requirements of 7.3 and 5.4 mg/d which can be rounded to 7.5 and 5.5 mg/d. Assuming a normal population distribution, Population Reference Intakes of 9.5 and 7 mg/d can be derived with Lowest Threshold Intakes at 5 and 4 mg/d for men and women respectively.

In reality requirements may be lower; in adult males zinc balance can be maintained on intakes of 5.5 mg/d but, since on a prolonged intake of 3.4 mg/d negative balances ensue, the above figures would seem prudent and practical on the basis of present evidence.

Children

Better information not being available, requirements have been calculated factorially [12].

In children 6-11 m, average faecal, sweat and urinary losses are estimated to amount to about 0.1 mg/kg body weight/d, and a growth increment has been based on a lean tissue zinc content of 30 mg/kg. Absorption of dietary zinc is taken as 30%, giving an average requirement, and 30% is added for individual variation to give the PRI.

For children from 1 year of age onwards, similar calculations have been made, interpolating values for basal losses between these for adults and infants, plus increments for growth, assuming 30% absorption. The values given are probably on the generous side.

Pregnancy

The extra zinc accumulated during the last trimester amounts to about 0.8 mg [13]. It is possible that there is more efficient absorption, but even so it might be thought that there would be a need for a raised dietary intake in late pregnancy. In reality this appears not to be so; pregnant women do not increase their customary intake, and there is no benefit from zinc supplements [14]. Healthy women seem to be able to adapt metabolically to transfer an adequate amount of zinc to the fetus. No additional recommendation is therefore made for pregnancy.

Lactation

It is possible that the absorption of dietary zinc may increase during lactation, but there is no good evidence that it does. An extra dietary intake of 5 mg/d is proposed to cover the amount of zinc produced in the milk.

Summary

(mg/d)

Adults	Males	Females
Average Requirement	7.5	5.5
Population Reference Intake	9.5	7
Lowest Threshold Intake	5	4

Population Reference Intakes of other groups (mg/d)

Age Group		PRI
	6-11 m	4
	1-3 y	4
	4-6 y	6
	7-10 y	7
Males	11-14 y	9
	15-17 y	9
Females	11-14 y	9
	15-17 y	7
	Pregnancy	7
	Lactation	12

References

1. Vallee B, Galdes A. (1984). The metallobiochemistry of zinc enzymes. *Advanc Enzymol Relat Areas Mol Biol*, **56**, 283-430.

2. Hambridge KM, Casey CE, Krebs NF. (1986). Zinc. In: Mertz W. ed. *Trace elements in Human and Animal Nutrition*. 5th ed. Vol 2. New York: Academic Press, 1-137.

3. Struhl K. (1989). Helix-turn-helix, zinc-finger and leucine-zipper motifs for eukaryotic transcriptional regulatory proteins. *Trends Biochem Sci*, **14:** 137-140.

4. Jackson MJ. (1989). Physiology of zinc: general aspects. In: Mills CF, ed. *Zinc in Human Biology*. London: Springer Verlag, 1-14.

5. Taylor CM, Bacon JR, Aggett PJ, Bremner I. (1991). Homeostatic regulation of zinc absorption and endogenous losses in zinc-deprived men. *Am J Clin Nutr*, **53:** 755-763.

6. Aggett PJ. (1989). Severe zinc deficiency. In: Mills CF, ed. *Zinc in Human Biology*. London: Springer Verlag, 259-279.

7. Anonymous. (1989). Does zinc supplementation improve growth in children who fail to thrive? *Nutr Rev*, **47:** 356- 358.

8. Gibson RS, Vanderkooy PDS, MacDonald AC, Goldman A, Ryan BA, Berry M. (1989). A growth limiting, mild zinc-deficiency syndrome in some Southern Ontario boys with low height percentiles. *Am J Clin Nutr*, **49:** 1266- 1273.

9. Yadrick MK, Kenney MA, Winterfeldt EA. (1989). Iron, copper and zinc status: response to supplementation with zinc or zinc and iron in adult females. *Am J Clin Nutr*, **49:** 145-150.

10. Milne DB, Canfield WK, Mahalko JR, Sandstead HH. (1983). Effect of dietary zinc on whole body surface loss of zinc: impact on estimation of zinc retention by balance method. *Am J Clin Nutr*, **38:**181-186.

11. King JC, Turnlund JR. (1989). Human zinc requirements. In: Mills CF, ed. *Zinc in Human Biology*. London: Springer Verlag, 335-350.

12. Hambridge KM. (1991). Zinc in the nutrition of children. In: Chandra R, ed. *Trace Elements in Children*. New York: Raven Press, 65-77.

13. Aggett PJ. (1989). Extra zinc in pregnancy. *Contemp Rev Obstet Gynaecol*, 181-189.

14. Mahomed K, James DK, Golding J, McCabe R. (1989). Zinc supplementation during pregnancy: a double blind randomized controlled trial. *Br Med J*, **299**: 826-830.