ZINC: A MINI REVIEW

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Introduction

Zinc was used in Rome and China more than 2,000 years ago as a component of brass and was first smelted from zinc ore in India in about 1200AD. The main zinc mineral is sphalerite which contains up to 67% zinc. Deposits containing zinc form from hydrothermal fluids generated within the earth and may be trapped to form veins or volcanogenic deposits under the sea. Some are forming today under the ocean off Papua New Guinea and Canada. Australia ranks first in the world in economic zinc resources because of the development of large zinc-lead-silver mines(1).

Contrary to the popular belief that zinc deficiency cannot occur in any largely meat eating population, studies have revealed that this deficiency is common in infants, children, adolescents and the elderly, not only in affluent but also in developing countries. Zinc is an essential trace mineral second only to iron. It is present in all organs, tissues, fluids and secretions of the human body with approximately 90% found in skeletal muscle and bone. Many homeostatic mechanisms require zinc. It plays an important role in zinc containing proteins including a large number of zinc dependent enzymes. Zinc is needed for growth, normal development and DNA synthesis to name a few.

Zinc is well known for its therapeutic activities via the antioxidant defence system and the immune system with results seen in the skin, eyes, the digestive, respiratory and even the cardiovascular system. Zinc promotes lipogenesis and potentiates insulin induced glucose transport(2). Less well known possibly are its benefits in cognitive development and function, neuropsychological behaviour, short term memory and motor development(3).

Food Sources of Zinc

Suboptimal zinc status has been recognised in both less developed and industrialised countries. The cause in many cases may be inadequate dietary intake due to poor food choices or protein/calorie malnourishment, but the importance of processing and the role of inhibitors of zinc absorption need to be recognised too. Zinc is readily absorbed in the upper small intestine from meat such as beef, lamb, turkey, chicken and pork. It is found in its highest levels in oysters and it is also present in lobster, clams, crab and all fish. All dairy products contain some zinc as do eggs.

Zinc is found in wheat, wheatgerm and bran, corn, oats, rice, buckwheat and especially rye. Garbanzo beans, soybeans, lentils, kidney, navy, pinto and lima beans all provide some zinc. It is very low in fruit and vegetables except broccoli, green beans and peas, and baked potato. While zinc is found in pumpkin and sunflower seeds, a lot would need to be consumed to provide the daily recommended daily intake (RDI)(4).

While it appears easiest to maintain zinc levels by following an omnivorous diet, a vegetarian diet where inclusion of whole grains and legumes occurs can allow zinc requirements to be met.

Bioavailability and Absorption

Zinc is highly bioavailable from human milk(5). When complexed with histidine this can provide 30—40% greater uptake of zinc compared to zinc sulphate(6). Citrate, methionine and EDTA are known to have positive effects on zinc absorption, whereas zinc carbonate and oxide are insoluble and poorly absorbed.

Phytates, present in foods like cereals, corn and rice, strongly inhibit its absorption, whereas most proteins have a positive effect. Iron too, if given in the same supplement, will have a negative effect on zinc absorption, as does calcium(7,8).

Cadmium competes with zinc for binding sites on metallothionein, which is important in the storage and transport of zinc during development(9).

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Toxicity and Dosages
Much has been made of the toxicity of zinc in the popular press, but the ingestion of 100—300 mg zinc/day that needs to be consumed to cause toxicity symptoms such as nausea, vomiting, epigastric pain and lethargy, rarely occurs. The RDI of many countries is from 9—15 mg elemental zinc per day. It would mostly be in the combining of several supplements that one would have to watch for toxicity. However, practitioners need to be aware that even lower levels of zinc closer to the RDI, may interfere with copper utilisation and adversely affect HDL cholesterol concentrations[10].

Research Overview
Studies of zinc have been ongoing since 1961, but are marked by in an accurate measure of zinc status. While measuring serum zinc is convenient and a small but important portion of body zinc is found there, mainly bound to plasma protein, zinc is primarily found intracellularly[11]. Notwithstanding this methodological difficulty, a significant number of earlier animal studies followed by well designed, human trials have taken place and their results cannot be ignored.

Studies in infants and children have focussed on zinc in the areas of growth and immune protection. In 98 Chil- ean children, aged 27—50 months, ‘from low socio-economic conditions’, 10 mg zinc per day resulted in the boys gaining some height and mid-arm muscle area. Both boys and girls had reduced rates of parasite reinfestation[12]. However, in a Mexican study of 219 preschoolers, 20 mg zinc methionine had no effect on growth, but there were fewer episodes of disease including diarrhoea[13].

In an earlier study in Papua and New Guinea, it was found that chronic malnutrition led to stunting and was exacerbated in the older children, aged 72—120 months, by zinc status less than two-thirds of the FAO/WHO recommendations[14]. The results of studies of single nutrient deficiencies such as zinc remain inconsistent, however, multiple micronutrient deficiencies remain consistent in developing countries.

A 2001 study of Mexican children aged 8—14 months confirmed that infants supplemented with 1.5 times the RDI of vitamins A, D, E, K, C, B1, B6, B12, riboflavin, niacin, biotin, folic acid, pantothenic acid and iron, zinc, iodine, copper, manganese and selenium had significantly greater length gains when the supplements were taken under 12 months of age. The differences in length gains were not significant, however, in those initially aged more than 12 months[15].

An important trial of 141 Bangladeshi infants and children aged 6 months to 3 years received doses of zinc from 1.5 mg/kg for 15 days, 6.0 mg/kg for 15 days or 6.0 mg/kg for 30 days. The results showed that mortality was higher in children that received 6.0 mg/kg zinc as opposed to those who received 1.5 mg/kg. The researchers concluded that ‘high dose zinc supplementation regimens … could contribute to increased mortality in severely malnourished children’[16].

Few studies have directly addressed the effects of zinc deficiency on behaviour (see Table 1), however, in a small but well constructed study of 85 Guatemalan in- fantst (aged 6—9 months, 10 mg zinc sulphate given daily for up to 7 months resulted in their sitting up and playing more than in the unsupplemented infants. They also cried and whined less[17].

The exact mechanisms of how zinc deficiency affects cognitive development are still not clear, but it is known that zinc containing neurons exist as a subset of glutamatergic neurons in the forebrain. These are interconnected with most of the cerebral cortices and limbic structures[18]. Caution, however, is called for in supplementing with zinc alone as evidenced by the trial of 150 infants aged 1 month who received 5 mg elemental zinc a day for 5 months, only to find that the results were slightly lower scores on the mental development index of the Bayley Scales than for the placebo group[19].

Certainly in the light of the available information, routine zinc supplementation cannot yet be recommended in pregnancy or for infants[20]. While extensive work has been carried out on animals indicating zinc deficiency leads to poorer memory, reduced activity and impaired learning and so on, much more research still needs to be carried out in human trials[21].

Both zinc and melatonin are essential in the immune system. In novel work in mice, a significant correlation was found between zinc and thymic hormone after two treatments of melatonin by injection. The researchers also suggested that interleukin-2 may participate in the action of melatonin, via zinc, on thymic functions in mice[22].

Zinc deficiency is common in many digestive disorders and there is now enough evidence to confirm the effic- acy of zinc supplementation in diarrhoea[23]. In those patients in remission from Crohn’s disease or who have suspected coeliac disease, zinc levels have been found to be suboptimal[24,25]. Other interesting recent research has shown that copper, zinc-superoxide dismutase may play a primary protective role against ultraviolet induced injury of human keratinocytes[26].
A final remark on zinc is that in 334 Canadian women with fibrocystic breast disease, body mass index, lower protein, niacin and zinc were found to be associated with the disease\(^{[27]}\).

**Conclusion**

Whether zinc is needed in the clinic setting for eczema, psoriasis, a sore throat, infertility or part of the treatment of macular degeneration or benign prostatic hypertrophy (BPH), it should never be overlooked. In fact, specifically looking for and expecting to find a zinc deficiency in every patient from neonates to the elderly would be more beneficial, whether that is in Australia or India.

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### Roles of Zinc in the Central Nervous System (CNS)

- Protein structure (zinc finger)
- Enzyme activity (catalytic site)
- Neurotransmitter action (ligand gated ion channels)
- Hippocampal function (mosaic fibre system)

### Extra CNS Influences of Zinc on CNS Functions

- Neurotransmitter precursor production (liver)
- Hormone/growth factor transport and receptor binding
- Receptor binding (GH, NGF)
- Hormone/toxicant metabolism (liver, testes)
- Energy supply (pancreatic insulin production)

### Indirect Influences of Zinc on CNS Functions

- Adrenocortical activation due to starvation
- Altered tissue trace metal content, especially copper
- Smaller body size due to reduced food intake/growth especially in concert with other deficiencies
- selective mortality

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**Table 1. Potential mechanisms of zinc deprivation effects on behaviour.**\(^{[27]}\)

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