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Zinc bioavailability to humans*

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The theme of zinc bioavailability in humans has become topical, given the demonstration of human zinc-deficiency[26]. There are a number of extensive reviews of the topic[2,20,31,32]. This review treats issues of zinc's biological availability as related to *humans* and *human dietetics*.

Intestinal absorption of zinc. The intestinal absorption of zinc is homoeostatically regulated and subject to influence by intraluminal factors. Figure 1 illustrates the routes of transport and mechanisms of regulation for zinc's absorption by intestinal cells. In the lumen, zinc is separated from the matrices of foods by mechanical and digestive processes, then possibly bound by a low-molecular-weight binding-species of pancreatic origin[1,11]. The cellular uptake of zinc is a carrier-mediated, saturable process[9,30]. The induction of metallothionein, an intracellular sulfhydryl-rich metal-binding protein is the basis for intestinal regulation of zinc movement. Elevation of metallothionein levels leads to sequestration of zinc within the intestinal cell[19]. Transfer of zinc from the enterocyte to the plasma is the rate limiting process in zinc absorption[9], and probably an energy-dependent process. The major route for excretion of endogenous zinc is pancreatic secretion[22].

In isotopic studies in human experiments, fractional absorption of zinc has ranged for 43 to 69 per cent while it ranges for 14 to 41 per cent for meals[32], providing evidence that dietary factors condition absorptive efficiency from the human diet.

Definition and concept of nutrient biological availability. The use of the term 'biological availability' with respect to zinc in human diets was introduced in 1973, in conjunction with calculations of adequate dietary intakes from distinct regional cuisines[29,35]. For most purposes, bioavailability has been synonymous with fractional absorption by the intestine[3,31]. However, a strong case has been made for a more ample definition[20]: 'Bioavailability is the proportion of a nutrient in food which is absorbed and utilized'; by utilization is meant, 'the process of transport, cellular assimilation and conversion to a biologically active form(s)'. In experimental

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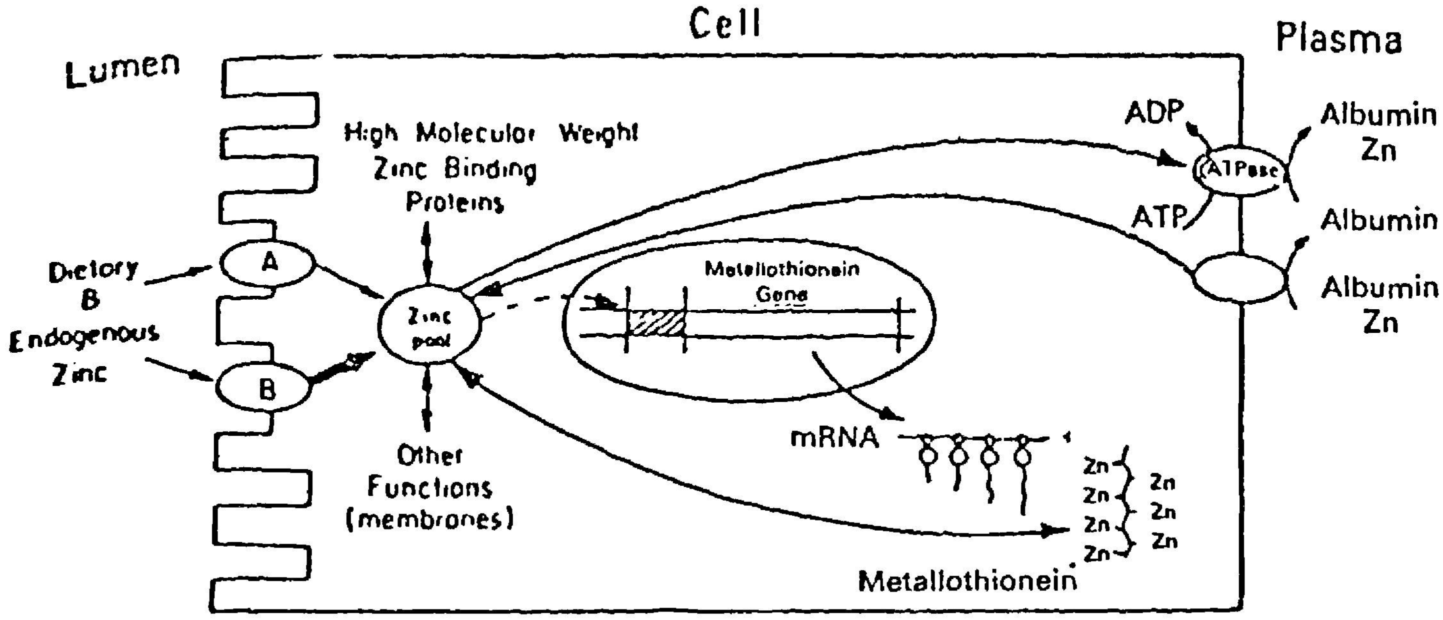


Fig. 1. *Schematic representation of zinc absorption by intestinal cells.* Carrier-mediated zinc transport at the brush border membrane is shown as A and B. Transport when an adequate amount of zinc is in the diet is shown as A, while the apparent increase in transport observed when the dietary supply is low is shown as B. Interactions of zinc with intracellular macromolecules are indicated as is the regulation of the metallothionein gene by dietary and plasma zinc. The active transport step is shown at the basolateral membrane. Transfer of cellular zinc to and from plasma albumin is also shown. After Solomons & Cousins, 1984[32]. Reproduced with permission.

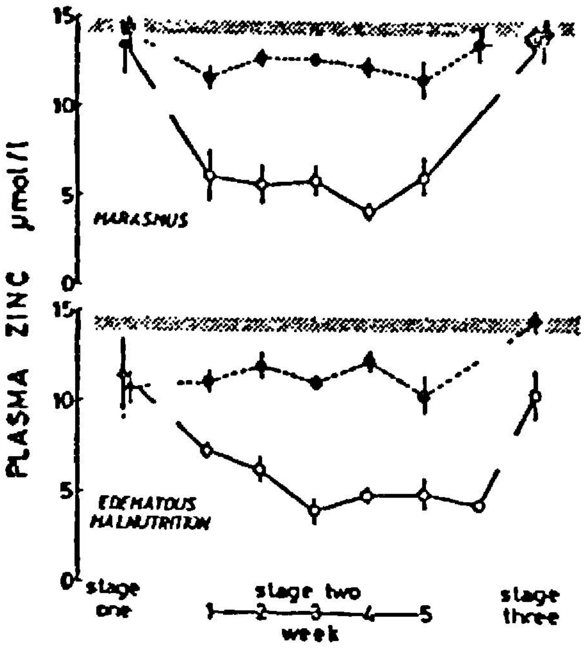
animals, haemoglobin repletion in anaemic rats[23] or reversal of pancreatic degeneration in selenium-deficient chicks[4] have served as indices of iron and selenium bioavailability with *utilization* as the definitive index. In studying repletion of platelet glutathione peroxidase in Finnish men fed selenium of various dietary sources a conscious transfer was made of this paradigm to human bioavailability studies[12]. In surveying the literature on human zinc biology, several studies are found in which an index of transport, tissue incorporation or growth have been measured in the context of long-term feeding of one or another diets contrasting in chemical characteristics.

Dietary factors and zinc bioavailability to humans. Our discussion here concerns observations in human subjects in which some index of zinc storage, transport or function has been evaluated over time in response to a specific dietary treatment. Many substances have been classified as enhancers or inhibitors of zinc bioavailability in experimental animal studies or human metabolic balance experiments[12,20,31,32]. Of these dietary factors, suitable observations have been made in people with human milk, unrefined cereals, soya-based diets, and inorganic iron.

Human breast-milk. In studies from Japan[21] and Denver, Colorado[15] comparing plasma zinc levels of breast- and bottle-fed infants at 3 or 6 months of life, circulating zinc concentrations were found to be significantly higher in breast-fed cohorts, despite a lesser net content of zinc in the breast-milk diets.

Dietary fibre and phytate. There is sufficient evidence from animal experiments that phytic acid and dietary fibre components are the major inhibitory factors that influence zinc availability in unrefined cereal grains[5,10]. When fed to volunteers in metabolic studies, whole-wheat flatbreads produced negative zinc balance[28]. Growth failure and altered zinc kinetics were shown in adolescent boys in rural Egypt consuming an unleavened flatbread[25]; evidence for a detrimental effect of this high-fibre, high-phytate food on zinc bioavailability was the dramatic growth spurt seen when a zinc-rich hospital diet was fed to these subjects.

Soyabean protein foods. When soya, a phytic acid-rich food, is fed to humans as a sole source of dietary protein, zinc appears to be less available than from non-soya-based foods. This has



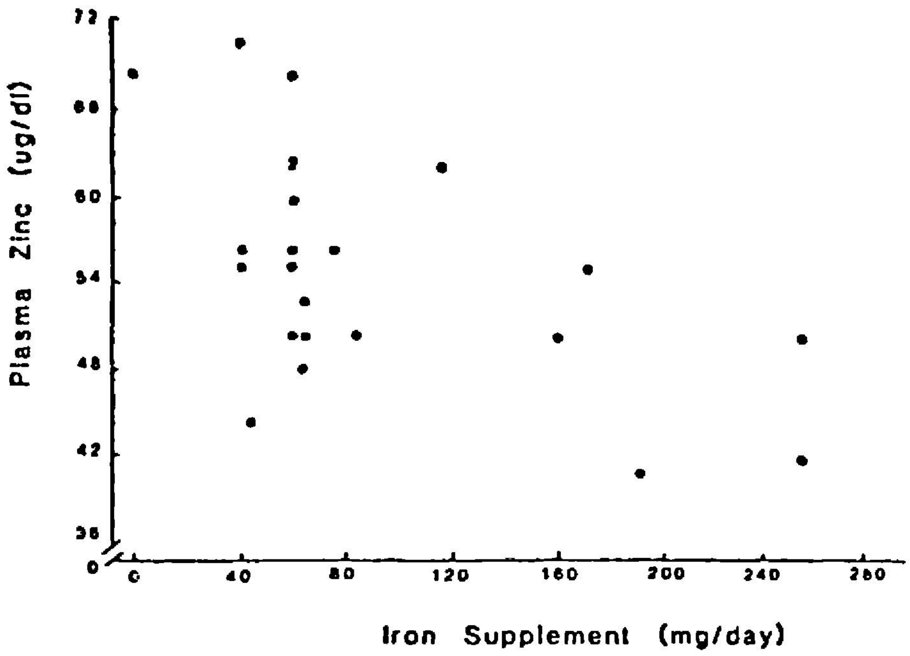


Fig. 2 (Above, left). *Plasma zinc concentration during recovery from severe malnutrition.* The upper graph for children with an admission diagnosis of marasmus and the lower graphs for children with edem malnutrition. △ and ▲, maintenance diet; ⊕, cow's milk based formula; O, soya protein based forn □ and ■, mixed diet. The open symbols are for children given the soya diet and the closed symbol those given the cow's milk diet. The shaded horizontal bars represent the mean ± SEM for the co children. Vertical bars show SEMs. From Golden & Golden (1981)[13]; reproduced with permission.

Fig. 3 (Above, right). *Plot of plasma zinc concentration at 9 months of gestation versus the level of pre supplementation.* From Hambidge *et al.*, 1983[14]; reproduced with permission.

been proven true for malnourished Jamaican children fed soya- and milk-based reco diets[13] (Fig. 2), and healthy American infants fed milk or soya formulas[7,8]. Circulating levels were lower in soya-fed subjects in all studies, and growth rates lagged in the Jama children's recoveries.

Progressive reduction was found in plasma and neutrophil (but not erythrocyte) zinc leve adult men who were switched from their usual mixed animal-protein diets to soya diets 1 months[6].

Inorganic iron. In 1970, a competitive interaction of chemically-similar ions was described[17]. and zinc are two such metals[16,24]. Several long-term experiences in humans suggest an effe high Fe/Zn ratios on circulating zinc transport. When marginal zinc intakes (< 3.5 mg d were fed to adult volunteers, 20-mg daily intakes of iron (Fe/Zn ratios = 5.7:1) allowed pla zinc levels to be maintained about 70 µg/dl, whereas with iron intakes of 130 mg (Fe ration = 48:1) plasma zinc concentration was reduced to below 70 µg/dl[27].

Cow-milk-based infant formulas, with and without added iron, were compared as to t effects on plasma zinc levels after 1 or 2 months of feeding; the Fe/Zn rations of 0.4:1 and produced significantly different mean plasma zinc levels, with mean concentrations being lo in the group fed the high-iron diet[7,8]. High iron contents of milk-based formula may accentuate the effect of a low zinc content, as suggested by the poorer growth of infants fe iron-fortified diet without supplementary zinc[34].

In two recent studies of pregnant women, inverse associations between circulating leve zinc and the amount of iron consumed as part of the prenatal vitamin-mineral supplement regimen were encountered. In Denver, Colorado in the 3rd trimester, higher iron intakes clearly correlated with lower plasma zinc (Fig. 3)[14]. Throughout the course of pregna consistently lower mean serum zinc concentrations were found in the cohort of women ta more than 30 mg of iron supplement daily[2]. It has been noted that many over-the-cou nutrient supplement preparations on the market have Fe/Zn ratios well over 3:1 and somet as high as 25:1[33]. Thus, in situations in which the tendency is to prescribe abundant iron in the diet, infancy and pregnancy, longitudinal studies suggest that depression in zinc transport in the blood can be the consequence due to poor bioavailability of the zinc.

Conclusions. The extent of our knowledge related to human zinc biology from experiments or observations conducted directly in man is limited, specifically if the more ample definition of nutrient bioavailability[18,20] incorporating a concept of nutrient *utilization* is applied. In the present survey, in which effects of dietary factors were evaluated in terms of either zinc transport or tissue incorporation *in vivo*, or growth, enhanced zinc biological availability from breast-milk and reduced bioavailability of zinc of high-fibre diets, soyabean protein diets and non-haem iron can be demonstrated. Further studies using a definition of availability that goes beyond simple intestinal uptake are needed to refine further our knowledge for human diets.

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Zinc in pregnancy

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Animal reproduction involves modifications in the metabolism of macro and micro-nutrients, because there is a need to meet the demands of production as well as those of maintenance. In this paper phenomena of Zn (zinc) supply and metabolism during gestation are presented.

The element zinc fulfils essential functions in reproduction in the main as a constituent or activator of enzymes and hormones. Functions of Zn in connection with the onset and efficient completion of parturition[3] and with the antibacterial activity of the amniotic fluid[20] have been unrecognized until recently. To meet the requirement resulting from these functions not only the quantity of dietary Zn plays a role, but also its utilization which may be influenced by numerous factors such as absorption, intermediate metabolism, excretion and interactions with other dietary constituents.

Zn absorption in pregnancy. The elevated requirement for Zn in the case of reproduction is met not only by higher feed intake, which is not so marked as during lactation, but also by an increased absorbability of dietary Zn which results at least partially from hypertrophy of the intestine especially in the late stages of pregnancy[2]. When the Zn supply was adequate, using *in vitro* experiments with everted intestinal sacs an increased Zn adsorption at the intestinal wall and a greater Zn absorption into serosal solution of pregnant rats in comparison with non-pregnant was demonstrated[22]. There was a sharp increase in absorption as pregnancy advanced in parallel with the growing accumulation of Zn in reproductive products[24]. A short time before parturition the absorption decreased. The decline in Zn absorption continued during lactation. Similarly, in pregnant sows, an increased apparent Zn absorption (intake minus faecal excretion) was found, which was again reduced shortly before parturition, perhaps caused by hormonal changes leading to parturition[13].

Super-retention and tissue distribution during pregnancy. In an experiment with sows a positive Zn retention in pregnant animals appeared only in the case of sufficient supply with Zn[13]. In this case the pregnant sows retained a greater quantity of zinc in reproductive organs and fetuses. The quantity retained by the reproducing organism exceeding the accumulation in conception products is defined as super-retention or as gravidity anabolism. This phenomenon is already known for nitrogen[15] and other trace elements, especially copper[14]. In experiments with pregnant rats such an anabolic effect could be demonstrated only in liver[21]. In comparison