

The Nutritional Relationships of Zinc

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Zinc was discovered to be essential for the growth of living organisms in 1869. The suspicion that zinc deficiency occurs in man is relatively recent. In 1963, studies reported by Prasad and co-workers on Iranian men suffering from dwarfism and hypogonadism found that nutritional zinc deficiency was a causative factor in these disorders.^{1 2 3} Since that time zinc has gained a greater recognition for its role in human health and has stimulated extensive research. It is now known that zinc is essential to over 100 enzymes in the body. Perhaps one of the most important discoveries is zinc's involvement in the synthesis of RNA.

Distribution

The highest concentration of zinc is found in the choroid of the eye and optic nerve, followed by the prostate, bone, liver and kidneys, muscles (zinc content varies with colour and function of muscles), heart, spleen, testes, brain, and adrenals. The skin also has a high concentration of zinc and can often be a sensitive indicator of zinc status. A zinc deficiency can adversely affect any of these organs.

Zinc Evaluation Through Tissue Mineral Analysis (TMA) of Human Hair

Hair TMA testing can be a good method of assessing zinc status and requirements in individuals. Even though tissue mineral levels in hair are not sensitive to acute zinc depletion, which is rare, it is considered one of the best methods for determining long-term nutritional zinc status.^{5 6 7} Since zinc is an intracellular element, it is agreed by most authorities that plasma, serum, and erythrocyte levels are not sensitive indicators of zinc status.^{8 9 10 11} As with most trace elements, the blood levels are maintained at the expense of tissue and are therefore, the last to reflect a chronic mineral deficiency. A low level of zinc found in the serum or plasma may indicate a deficiency, but it may

also indicate tissue redistribution.¹² The normal range of zinc in the hair has been reported between 15 and 22 milligrams percent,⁴ the ideal being 20 milligrams percent.

Manifestations of Zinc Deficiency Absolute or Relative

Manifestations of zinc deficiency will vary from one individual to another. This is true of almost any nutrient, and can be explained by recognizing that two types of a deficiency state can occur, either a *relative deficiency*, or *absolute deficiency*. An absolute deficiency develops as a result of inhibited absorption accompanied by a concurrent increase in zinc excretion or utilization. TMA patterns usually reveal a low tissue zinc (less than 12 mg.%). An absolute deficiency of zinc can be contributed to by hypoadrenocorticism, hyperthyroidism and other endocrine factors.

A relative deficiency develops as a result of zinc loss from tissue storage (compartmental displacement), without an increase in excretion. A relative deficiency is seen on TMA results where the zinc level is within the normal range but relatively low when compared to an antagonistic mineral such as copper, or cadmium (low Zn/Cu, low Zn/Cd). A relative deficiency state can be contributed to by adrenal insufficiency, hypothyroid, and hyperparathyroidism. As an example, studies performed on a group of pregnant women compared to a control group revealed that urinary zinc excretion was not significantly different from nonpregnant controls except during certain months. Trace element analysis of the hair on both groups revealed a gradual increase in tissue zinc levels in the test group toward the end of the pregnancy.¹⁸ It is well known that copper levels rise during pregnancy as well as during oral contraceptive and estrogen therapy.¹⁹ This is usually reflected on TMA studies²¹ and would apparently indicate that copper causes a relative deficiency rather than absolute deficiency of zinc. This

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may be explained by the metabolic effects of copper. First, copper is considered an anabolic mineral, therefore, it may increase the metabolic requirements for zinc which is also required for anabolic processes. Secondly, an increase in parathyroid activity is known to increase zinc retention,²¹ and suppress thyroid and adrenal activity²² which would contribute to a decrease in zinc excretion. Both the parathyroid and thyroid glands are affected by copper. Any of these conditions would produce a relative deficiency of zinc by producing compartmental displacement. Even though the TMA zinc level may be normal, the low zinc to copper ratio (less than 8 to 1), would indicate an increased requirement for zinc.

Conditions Associated with Zinc Deficiency

One of the most serious manifestations of zinc deficiency is seen in acrodermatitis enteropathica, a genetic disorder that occurs in children.²⁴ Serum and hair zinc levels are both found low in children with this condition and who respond well to zinc supplementation. This condition is associated with an absolute zinc deficiency.

Zinc deficiency has been found in patients with lupus erythematosus, scleroderma, psoriasis, skin blemishes and rashes, and slow wound healing.

Sickle Cell Anemia

Zinc deficiency is seen in people suffering from sickle cell anemia.²⁷ It has been found that in sickle cell disease excessive calcium accumulates within the red blood cells contributing to their deformity. Zinc has proven beneficial due to its effect of decreasing calcium infiltration into the erythrocytes.

Diabetes

Zinc is also known to be required for insulin storage. Zinc depletion has been found to occur in some forms of diabetes, most notably juvenile type. Individuals with adult onset diabetes also show a need for zinc which is due to increased requirements as a result of increased anabolic demands.

Anorexia Nervosa

Taste disorders and a loss of smell is common with zinc deficiency.²⁸ Individuals suffering from anorexia nervosa have been found to have relative zinc deficiencies with a very low zinc to

copper relationship. Apparently a relative zinc deficiency produces abnormal taste and smell particularly to protein. This phenomena is not often seen in absolute deficiency states. In fact, individuals with an absolute deficiency of zinc have a greater desire for protein. This could be explained by the difference in the hydrochloric acid status of these individuals.

Viruses

Zinc has an antiviral effect, particularly on many forms of rhinoviruses. In vitro it has been found to affect poliovirus in high concentrations. The antiviral effects of zinc have been found to be even more effective when given in conjunction with vitamin A, and magnesium. Zinc deficiency is associated with a decrease in immune response and increased susceptibility to viral infections.

Zinc Deficiency and Visual Disturbances

Relative deficiencies of zinc can cause visual changes known as dyschromatopsia, a disturbance of the red/green color axis²³ characterized by an inability to distinguish easily between certain shades of greens and blues. Dyschromatopsia is commonly seen in individuals with low tissue zinc to copper ratios.

Striae (Stretch Marks)

The integrity of the skin depends upon adequate levels of zinc due to its involvement in protein synthesis and collagen production. Striae, commonly known as stretch marks, has been found to be associated with zinc deficiency. Striae occur due to a breaking of skin collagen tissue resulting in scar formation. This often develops during pregnancy, weight gain (seen in body builders), and obesity.²⁵ Mechanical strain on the skin can produce stretch marks and may be seen around the breasts of zinc deficient women. Clinically, striae can indicate a relative or absolute deficiency of zinc by its colour. A relative zinc deficiency is associated with white, or silver striae. Red to purple striae are seen in individuals with an absolute zinc deficiency status, and is commonly associated with hyperadrenocorticism,²⁶ or prolonged corticosteroid therapy.

Fingernail White Spots

Pfeiffer described white spots that appear in the fingernails as being due to a zinc deficiency.²⁹ TMA research indicates that these are more likely to be copper toxic spots rather than zinc deficient spots. They are more commonly seen in individuals with relative zinc deficiency states rather than in those with an absolute deficiency. White spots in the nails are frequently seen in individuals with TMA zinc levels within the normal range, but relatively low in relation to copper. White spots are not often seen in individuals with tissue zinc levels as low as fifty percent of normal.

The following is a list of conditions observed through TMA studies over the past several years that have been associated with zinc deficiency. They are categorized according to either a relative (R), or absolute (A) zinc deficiency.

Pregnancy (R), Premenstrual Syndrome (R), Autism(R), A.I.D.S. (R), Candida (R), Eclampsia (R), Anorexia Nervosa (R), Post Partum Depression (R), Schizophrenia (R), Viruses (R), Fungus (R), Depression (R), Manic Depression (A), Arthritis Rh. (A), Sterility (A) (R), Retinal Disturbance (R), Ulcers (gastric) (R), Juvenile Diabetes (A), Skin Ulcers (A), Prostatic Hypertrophy (A), Diabetes, Adult Onset (R), Macular Degeneration (A), Ulcers (peptic) (A), Malignancies (with a high metastatic rate) (A), Malignancies (with a low metastatic rate) (R).

Factors Contributing to Zinc Deficiency

Drugs can produce a zinc deficiency by suppressing absorption, increasing excretion, or interfering with zinc synergists, such as vitamin B6 and magnesium. Etham-butal and isoniazid, antitubercular drugs, and diiodohydroxyquin, used for entamoeba histolytica, contribute to zinc deficiency. They particularly affect the eyes and can produce atrophy of the optic nerve, optic neuritis, and blindness. Nialamide and isocarboxazid are MAO inhibitors and are used as antidepressants. They are known to cause visual disturbances due to their antagonistic effect upon zinc metabolism. These drugs act by producing a sympathomimetic effect and therefore probably contribute to an absolute zinc deficiency. Anti-

inflammatories such as corticosteroids and diuretics such as thiazides are commonly used medications that can also adversely affect zinc status. Alcohol is known to produce a diuresis of zinc and increase iron absorption or retention. Diets high in phytates also decrease zinc absorption.

Minerals Antagonistic to Zinc

There are many nutritional factors that can affect zinc requirements either favourably or unfavourably. These include both vitamins and minerals. Figure 1 indicates the minerals that are antagonistic to zinc.^{13 14 15 16 17} Excessive intake or tissue accumulation of any one or combination of these trace elements can contribute to zinc deficiency by exerting either an absorptive or metabolic antagonistic effect. Excessive accumulation or toxicity of most of the antagonistic elements shown in Figure 1 can be treated with zinc therapy, especially the heavy toxic metals such as lead (Pb), Cadmium (Cd), and Mercury (Hg).

It should also be noted that excessive intake of zinc over prolonged periods can produce a deficiency of chromium (Cr), copper (Cu), iron(Fe), or manganese (Mn).

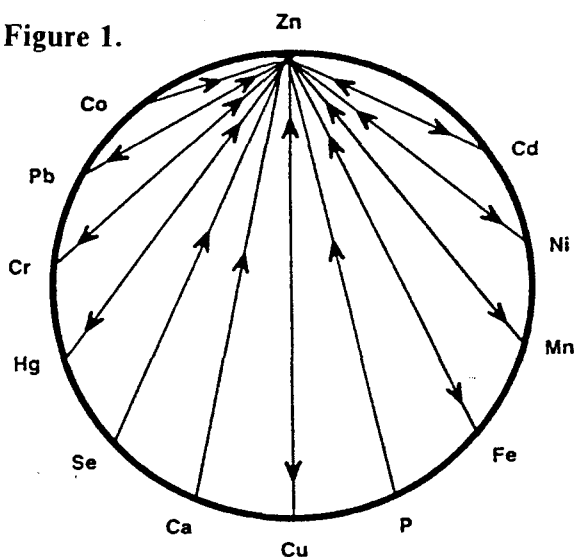
Vitamins Antagonistic to Zinc

Vitamins can also affect zinc status. Figure 2 indicates the vitamins that are considered antagonistic to the mineral zinc in higher than physiological dosages. Vitamin antagonism toward zinc can occur either directly or indirectly. As an example, vitamins E and B1 stimulate adrenal anabolic hormone production and can therefore produce a zinc deficiency by increasing its requirement during anabolism. Vitamin D, by increasing the absorption of calcium, can suppress zinc absorption. Vitamin D also decreases thyroid activity, and increases parathyroid activity, thus contributing to a relative zinc deficiency by decreasing its absorption. Inositol is a hexaphosphate derivative (phy-tate), and can also depress zinc absorption. As with the minerals, excessive zinc intake can also produce a deficiency, or increase the requirements of these vitamins.

Nutrients Synergistic to Zinc

Minerals that are synergistic with zinc

Figure 1.



include magnesium, manganese, iron and phosphorus.

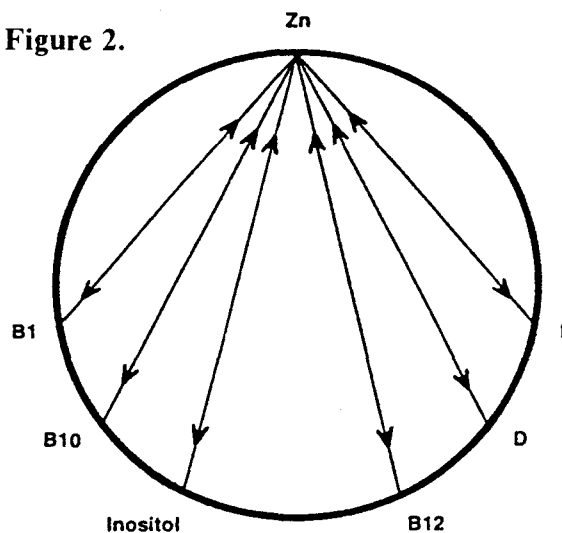
The following vitamins are considered synergistic to zinc: vitamin A, B6, B3, B5, B1, and vitamin E.

It should be noted that some vitamins and minerals appear as synergistic as well as antagonistic. Within a physiological range a nutrient can act as a metabolic synergist to zinc, but in higher amounts it can antagonize the metabolic functions and/or absorption of zinc. As an example, even though the mineral copper is antagonistic to zinc, it can also be considered synergistic to zinc metabolically, since both are required for normal collagen synthesis integrity.

Zinc Toxicity

The most recognized problem of zinc toxicity is its antagonistic effect upon copper. In absolute deficiency states tissue copper levels are often found low. The tissue zinc may only be 12 mg%, but relative to a tissue copper level of 0.5 mg% the zinc would be considered high by as much as 24 times relative to copper (ideal Zn/Cu=8). As an example, a patient developed a TMA pattern similar to this as a result of taking 300 milligrams of zinc for approximately two years. Initially he began taking 150 milligrams of zinc for prostatic hypertrophy. This improved the prostate condition so he continued the 150 milligrams for preventative purposes. About a year and a half later he developed prostatitis as a result of an infection, so he increased his zinc intake to 300 milligrams per day. His prostate disturbance

Figure 2.



did not improve, but grew progressively worse. It was not responding to antibiotics which he was also taking along with the zinc. His TMA results revealed a high zinc to copper ratio. He was instructed to discontinue the zinc and begin copper supplementation, which resulted in a marked improvement in his condition.

Excessive amounts of zinc is also known to contribute to, hypercholesterolemia, infections, anemia, and scurvy-like symptoms.

Zinc Requirements

The established minimum daily requirement for zinc in infants is 3-5 milligrams per day; for adult males, 15 milligrams; for adult females, 20 milligrams; and for lactating women, 25 milligrams per day. Individual requirements for zinc, however, depend upon many factors such as stress, medications, illness, and the type of diet a person is consuming (vegetarians have increased zinc requirements). Assessing zinc requirements should include these factors in addition to recognizing the effect of approximately thirty other nutrients upon zinc status.

Generally speaking, zinc supplementation should be approached with caution in absolute deficiency conditions which usually only require small amounts of zinc supplementation to produce a favourable response. However, in relative deficiency conditions, zinc requirements may be quite high, often several times the MDR. Response to zinc therapy can be greatly enhanced when synergistic and antagonistic nutrients are also considered.

In conclusion, TMA can be a very effective laboratory test for evaluating zinc status and requirements when assessed according to its physiological range with other nutritional factors. Other than through TMA testing, the only way to unconditionally determine a zinc deficiency is through response to therapy.

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