Zinc

Zinc deficiency

Zinc deficiency is a lack of sufficient zinc to meet the needs of biological organisms. It can occur in both plants and animals or soil. *Hypozincemia* is a condition where insufficient zinc is available for metabolic needs.

In plants, crops, and soils

Zinc is an essential micronutrient needed not only by people but also by crops. Almost half of the world's cereal crops are deficient in zinc, leading to poor crop yields. Many agricultural countries around the world are affected by zinc deficiencies. In China, zinc deficiency occurs on around half of the agricultural soils, affecting mainly rice and maize.

In India, zinc-deficient soils occupy almost 50% of the agricultural area and are a critical constraint on yield, but crops are highly responsive to zinc fertilization.

In Turkey, major yield and quality benefits in wheat have been obtained with the widespread use of zinc fertilizers, where half of the cereal growing land is zinc-deficient.

Research has shown that areas with zinc-deficient soils are often regions with widespread zinc deficiency in humans.

Causes

Hypozincemia is usually a nutritional deficiency, but can also be associated with malabsorption, diarrhea, acrodermatitis enteropathica, chronic liver disease, chronic renal disease, sickle-cell disease, diabetes, malignancy, and other chronic illnesses. It can also occur after bariatric surgery.

Zinc deficiency is typically the result of inadequate dietary intake of zinc, disease states that promote zinc losses, or physiological states that

require increased zinc. Populations that consume primarily plant based diets that are low in bioavailable zinc often have zinc deficiencies.

Diseases or conditions that involve intestinal malabsorption promote zinc losses. Fecal losses of zinc caused by diarrhea are one contributing factor, often common in developing countries. Changes in intestinal tract absorbability and permeability due, in part, to viral, protozoal, and bacteria pathogens may also encourage fecal losses of zinc. Physiological states that require increased zinc include periods of growth in infants and children as well as in mothers during pregnancy.

Signs and symptoms

Signs of zinc deficiency include hair loss, skin lesions, diarrhea, and wasting of body tissues. It is rarely recognized that lack of zinc can contribute to acne. Eyesight, taste, smell and memory are also connected with zinc. A deficiency in zinc can cause malfunctions of these organs and functions. Congenital abnormalities causing zinc deficiency may lead to a disease called *acrodermatitis enteropathica*.

One easily recognized sign which may be caused by zinc deficiency is white spots, bands, or lines on fingernails (leukonychia). An occasional white spot is usually evidence that the immune system overcame a bacterial or some other systemic infection, and is a positive, not negative sign. Some women may have multiple parallel white bands or lines on the fingernails marking menstrual cycles when marginal zinc deficiency was present.

Anorexia

Zinc deficiency may cause a decrease in appetite which can degenerate into anorexia or anorexia nervosa. Appetite disorders, in turn, cause malnutrition and, notably, inadequate zinc intake. Anorexia itself is a cause of zinc deficiency, thus leading to a vicious cycle: the worsening of anorexia worsens the zinc deficiency.

The use of zinc in the treatment of anorexia has been advocated since 1979 by Bakan. At least 15 trials showed that zinc improved weight gain in anorexia. A 1994 randomized, double-blind, placebo-controlled trial showed that zinc (14 mg per day) doubled the rate of body mass increase in the treatment of anorexia nervosa (AN). Deficiency of other nutrients such as tyrosine and tryptophan (precursors of the monoamine neurotransmitters norepinephrine and serotonin, respectively), as well as vitamin B1 (thiamine) could contribute to this phenomenon of malnutrition-induced malnutrition.

Cognitive and motor function impairment

Cognitive and motor function may also be impaired in zinc deficient children. Zinc deficiency can interfere with many organ systems especially when it occurs during a time of rapid growth and development when nutritional needs are high, such as during infancy. In animal studies, rats who were deprived of zinc during early fetal development exhibited increased emotionality, poor memory, and abnormal response to stress which interfered with performance in learning situations. Zinc deprivation in monkeys showed that zinc deficient animals were emotionally less mature, and also had cognitive deficits indicated by their difficulty in retaining previously learned problems and in learning new problems.

Human observational studies show weaker results. Low maternal zinc status has been associated with less attention during the neonatal period and worse motor functioning. In some studies, supplementation has been associated with motor development in very low birth weight infants and more vigorous and functional activity in infants and toddlers.

Diarrhea and pneumonia

Zinc deficiency contributes to an increased incidence and severity of diarrhea and pneumonia. Studies have shown that zinc treatment results in a 25 percent reduction in duration of acute diarrhea and a 40 percent reduction in treatment failure or death in persistent diarrhea.

The studies determined that a ten-day therapy of zinc treatment can considerably reduce the duration and severity of diarrheal episodes, decrease stool output, and lessen the need for hospitalization. Zinc may also prevent future diarrhea episodes for up to three months.

The current World Health Organization recommendation for diarrhea control includes the use of 20 mg per day of zinc supplementation for 10 to 14 days (10 mg per day for infants under the age of six months). A zinc taste test may have potential for diagnosing deficiency.

Dysmenorrhea

High dose of zinc, 30 mg 1-3 times a day, prevents dysmenorrhea.

Pregnancy and zinc deficiency

Zinc deficiency during pregnancy can negatively affect both the mother and fetus. Animal studies indicate that maternal zinc deficiency can upset both the sequencing and efficiency of the birth process. An increased incidence of difficult and prolonged labor, hemorrhage, uterine dystocia and placental abruption has been documented in zinc deficient animals. These effects may be mediated by the defective functioning of estrogen via the estrogen receptor, which contains a zinc finger protein. A review of pregnancy outcomes in women with acrodermatitis enteropathica, reported that out of every seven pregnancies, there was one abortion and two malfunctions, suggesting the human fetus is also susceptible to the teratogenic effects of severe zinc deficiency. However, a review on zinc supplementation trials during pregnancy did not report a significant effect of zinc supplementation on neonatal survival.

Vitamins A and D

Plasma zinc levels have been found to be dependent upon vitamins A and D. This suggests that a Vitamin A or D deficiency could cause a secondary zinc deficiency and that for treatment of zinc deficiency one should ensure adequate vitamin A and D intake.

Zinc and hunger

The influence of zinc on hunger is complex and likely depends upon the status of other nutrients, the developmental stage of the animal, and percentage body fat. Some research groups have argued for a role of zinc deficiency decreasing appetite, while others have shown zinc ingestion can reduce feelings of hunger by increasing leptin levels.

There is evidence that the way zinc influences hunger depends on the sodium/osmotic status of the organism, with low sodium/low zinc levels increasing hunger and high sodium/low zinc levels decreasing it. An organism with a low level of zinc has an increased susceptibility to hypo-osmotic stress and cell rupture. Thus if the osmotic pressure is too low the organism may be inclined to eat to raise osmolality and prevent osmotic shock. It should be noted that zinc is known to affect osmolality by increasing sodium retention.

Treatment

Zinc supplementation has been shown to reduce diarrhea prevalence and mortality in children younger than 5 years of age.

To combat zinc deficiency, five intervention strategies can be used:

- Supplementation using medicines
- Food fortification through the incorporation of zinc additives in food
- Dietary modification/diversification
- Genetic bio-fortification through plant breeding
- Agronomic bio-fortification through zinc fertilization.

These five intervention strategies may be used individually or in combination, depending on the setting, target group and degree of zinc deficiency.

The amount of zinc absorbed by the human body is a function of dietary intake of both zinc and phytate (a phosphate storage

compound that chelates zinc), because the ratio between these two substances affects the bioavailability of zinc. Meeting the needs for absorbed zinc requires an increase in the zinc content and/or a decrease in the phytate content.

Zinc deficiency-- A Cause of modern illness

Shifting from consumption of meat proteins to cereal proteins containing high levels of fibers known as phytates may precipitate a general increase in zinc deficiency. Other known causes of zinc deficiency in man include surgery, malabsorption syndrome, being an athlete, frequent ejaculation (most often by homosexuals), excessive alcohol intake, fasting, institutional diets, illegal drug use, chronic diseases (including sickle cell anemia, Wilson's disease, renal and liver diseases), lack of zinc in food crops grown in zinc depleted soils, a poor diet, dependence on processed foods, vegetarianism, and long term exposure to environmental toxins.

Continued increase in zinc deficiency may be dangerous to humanity because dietary zinc deficiency -- dependent upon severity and other factors -- can result in:

(a) Primary T-cell lymphocyte immune system dysfunction (failure to terminate incipient malignancies, viral and fungal infections),

(b) Inability to protect cell membranes from viruses, toxins, complement, and venoms,

(c) Poor appetite (particularly in the young and aged),

(d) Mental lethargy,

(e) Abnormal neuro-sensory changes,

(f) Chronic diarrhea,

(g) Growth failure (dwarfism),

(h) Vision problems,

(i) Fertility problems (including hypogonads, failure of sexual maturity, benign prostatitis in men, and menstrual cramping and bloating in women),

(j) Essential hypertension,

(k) Angina pectoris,

(l) Ischemia of effort,

(m) Delayed wound healing,

(n) Free radical damage,

(o) Frequent opportunistic infections,

(p) Scleroderma,

(q) Systemic scleroderma (including lethal pulmonary hypertension),

(r) Respiratory and skin allergies,

(s) Asthma,

(t) Premature aging,

(u) Loss of hair color,

(v) Anemia,

(w) Striae (stretch marks),

(x) Joint pain,

(y) Loss of taste,

(z) Birth defects.

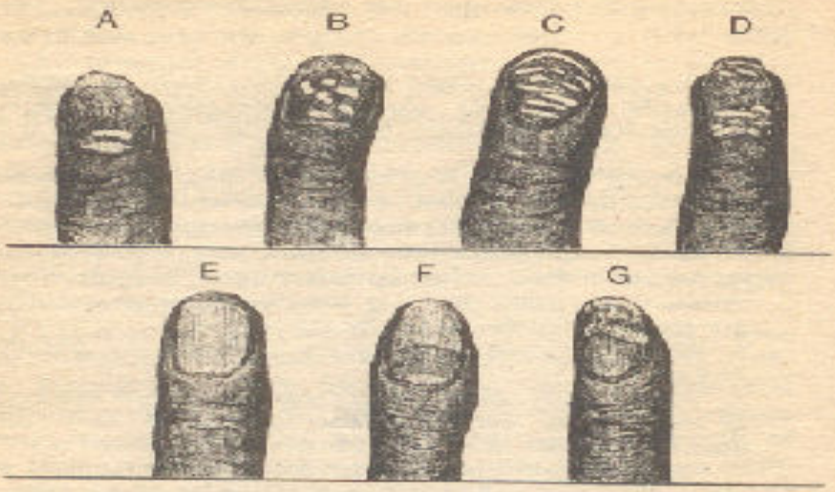
In chronic zinc deficiency, smoking tobacco can result in absent zinc being replaced with toxic cadmium from cigarette smoke eventually resulting in lung disease. Lead, cadmium, and mercury toxicity can be treated by displacing those elements by therapeutic doses of dietary zinc. It is probable that each of these disorders will respond to, be prevented by, or be cured by daily therapeutic doses of zinc (ten times the U.S. RDA 15 mg for zinc).

Humanity faces a bleak future filled with disease. Consequently, zinc may be far more valuable to humanity than the most precious of metals -- gold.

Signs of zinc deficiency

One easily recognized sign of zinc deficiency is white spots, bands, and lines on finger nails. An occasional white spot is usually evidence that the immune system overcame a bacterial or some other systemic infection, and is a *positive,* not negative sign. Some women will have multiple parallel white bands or lines on their fingernails marking menstrual cycles in marginal zinc deficiency.

According to some biomedical researchers, human zinc deficiency may be correctable only by a therapeutic intake of 100 to 150 mg zinc per day taken orally for a few months. Significantly exceeding 150 mg per day to correct serum zinc deficiency is rarely warranted, and often causes nausea and vomiting, and may have other deleterious effects on health, primarily through depletion of serum copper. Some researchers suggest adding trace amounts of copper and vitamin B-6 with supplemental therapeutic doses of zinc to help reestablish proper zinc serum levels.



Types of white spots on fingernails (leukonychia) seen in zinc-deficient patients

A. Isolated white spot originating from a period of fasting or altered diet. Yom Kippur fasting, or a day of anorexia can cause such a white spot. A back-packing trip (which usually does not include fresh red meat as a source of zinc) can also produce a white spot. A hospital stay of 5 days also caused a white spot indicating the low level of zinc in that hospital's diet.
B. Multiple white spots in the finger and toe nails of an eleven-year-old child whose serum zinc level was low and whose behavior was inappropriate.
C. Monthly white bands or menstrual white spots in a female pyroluric patient. Copper is high and zinc is low premenstrually when many women feel depressed.
D. White spots in the nail of a female pyroluric patient who ran out of zinc and vitamin B-6 after a 2½ month period of treatment. The center band of normal-appearing nail represents the period of zinc therapy.
E. Opaquely white nail of an older pyroluric patient who also had hypertension and elevated serum copper. The hypertension rsponds to zinc and vitamin B-6 therapy and the nail becomes normal pink in color.
F. Opaquely white nail after 3 months of zinc B-6 therapy.
G. White spot in a depression in the nail (Beau's Grove) caused by a virus infection with a high fever. Virus infections cause a loss of zinc via the urinary pathway and the altered metabolic rate of a fever results in the transverse groove.

Primary role of zinc ions

Most serum Zn^{2+} ions are used by the body to stabilize cell membranes and close pores in cell membranes. In vitro, Charles A. Pasternak, PhD, MD (Hon), of St. George's Medical Hospital, University of London, has found that increasing Zn^{2+} ion concentrations to be a novel and newly recognized form of host defense, because they strengthen cell membranes and protect them from damage from many cytotoxins, including viruses, and venoms.

Similarly, we have *some* evidence that oral intake of extremely large doses of ionizable zinc compounds can prevent injury and possibly death from potentially lethal cytolytic agents.

Three grams of zinc (from zinc gluconate) taken in four 750-mg doses per day with meals for a week has been successfully used to prevent severe tissue necrosis and possible death from a brown recluse spider bite in the navel of a 100-pound female adult. This treatment produced no observable side effects (neither nausea nor vomiting), rapidly eliminated systemic bloating and generalized pain, and resulted in rapid wound healing without scarring. However, if such extreme dosage is given in *health*, zinc toxicity *must always* be expected.

Excessive consumption of zinc over a long period can interfere with copper absorption and has reversible side effects, the most noticeable being anemia and neutropenia. Like overdoses of any nutrient, stopping or reducing dietary zinc supplementation has been reported to be corrective. On the other hand, many people carrying a burden of excess -- and potentially toxic – copper, may be beneficially adjusted by supplemental zinc.

Anti oxidant effects

Zn^{2+} ions are nature's strongest antioxidants, far more so than vitamins C and E, and much safer than selenium. Generally, therapeutic doses of zinc in *highly ionic forms* to treat diseases, wounds, burns, and

venomous bites are a fresh and promising area demanding further research.

Zinc Deficiency — Symptoms and Risks

Zinc is crucial to a healthy immune system, normal growth and overall health. Those with even a slight zinc deficiency may suffer from a variety of symptoms.

Zinc is an essential mineral that is involved in hundreds of bodily processes, including helping to protect the body from oxidative stress and repair DNA. While zinc is readily available in food, research suggests 2 billion people worldwide do not get enough zinc in their diet, and even in the U.S., 12 percent of the general population and 40 percent of the elderly population are at risk of zinc deficiency.

RDA of Zinc

The Institute of Medicine suggests the following Recommended Dietary Allowance (RDA) for zinc:

- Birth to 6 months – 2 mg
- 7 months to 3 years – 3 mg
- 4 to 8 years – 5 mg
- 9 to 13 years – 8 mg
- Females 14 to 18 years old – 9 mg (18 mg for those who are pregnant and 14 mg for lactating women)
- Females 19 years and older – 8 mg (11 mg for pregnant women and 12 mg for lactating women)
- Males 14 years and older – 11 mg

Zinc Deficiency Symptoms

Symptoms of a zinc deficiency may include slow growth, loss of appetite, and impaired immune function. In extreme cases, a zinc deficiency may cause:

- Loss of hair

- Impaired sense of taste or smell
- Diarrhea
- Impotence
- Hypogonadism in males
- Weight loss
- Mental lethargy
- Skin lesions
- Low insulin levels
- Rough and dry skin
- Slow wound healing

Recent research suggests that even a minor zinc deficiency can cause DNA damage.

According to the National Institute of Health, there are certain groups at risk of zinc deficiency, including:

- People with gastrointestinal disorders and diseases such as ulcerative colitis, Crohn' s disease, and short bowel syndrome
- Vegetarians
- Expectant and nursing women
- Infants over 7 months who are exclusively breastfed
- Those with sickle cell disease
- Alcoholics

Those who are most at risk of zinc deficiency should try to eat a healthy diet that includes rich sources of zinc such as: oysters, beef shank, zinc-fortified breakfast cereals, whole grains, pork tenderloin, cashews, yogurt, and baked beans. Breastfeeding women can also supplement their baby's diet with baby cereals that are fortified with zinc. A zinc supplement should also be considered for those at risk and the elderly.

Since many of the symptoms of zinc deficiency can be due to a variety of health conditions, those who feel they may suffer from a zinc deficiency should consult a physician.

Zinc deficiency impairs intestinal immunity

Epidemiological evidence to support a role for zinc in maintenance of the gut epithelial barrier and intestinal immunity is limited and difficult to interpret. In a double-blind, randomized, controlled trial of children with acute diarrhea, daily supplementation with elemental zinc reduced the risk of continued diarrhea by 21%, after controlling for stunting, age and baseline plasma zinc concentration, and also reduced the severity of the diarrhea, particularly in stunted children . The improvements in the growth of and reduction in diarrheal episodes in zinc-supplemented children were most striking in children who were moderately or severely malnourished although not necessarily zinc deficient.

Function of Zinc in the body

The mineral zinc is present in every part of the body and has a wide range of functions. It helps with the healing of wounds and is a vital component of many enzyme reactions. Zinc is vital for the healthy working of many of the body's systems. It is particularly important for healthy skin and is essential for a healthy immune system and resistance to infection. Zinc is one of the minerals men should never be without and has such a wide application in human health that everybody should ensure that they obtain enough of this humble trace element.

A vital enzyme, carbonic anhydrase, contains zinc. It is also essential for the activity of some enzymes and hence essential foe the life of the organism. Other enzymes viz. several dehydrogenases (alcohol, glutamic, certain pyridine nucleotide) and pancreatic carboxypeptidase contain zinc. It is chiefly excreted in urine.

Our body contains about 2-3g of zinc. There are no specific storage sites known for zinc and so a regular supply in the diet is required. Zinc is found in all parts of our body, 60% is found in muscle, 30% in bone and about 5% in our skin. Particularly high concentrations are in the prostate gland and semen. Men need more zinc than women

because male semen contains 100 times more zinc than is found in the blood. The more sexually active a man the more zinc he will require. The recommended amounts of zinc for adult men are 1/3 higher than those for women.

It is thought that zinc supplementation can help skin conditions such as acne and eczema, prostate problems, anorexia nervosa, alcoholics and those suffering from trauma or post-surgery. It is always better to seek the advice of an expert before taking any supplements. If you choose to take a zinc supplement you should not need more than the daily recommended amount unless medical advice says otherwise.

Only 20% of the zinc present in the diet is actually absorbed by the body. Dietary fibre and phytic acid, found in bran, wholegrain cereals, pulses and nuts, inhibit zinc absorption. Phytic acid forms a highly insoluble complex with zinc, which the body cannot absorb. Cooking processes can reduce the adverse effects of both phytic acid and dietary fibre on zinc absorption. Baking can destroy over half the phytic acid in whole meal bread.

Numerous aspects of cellular metabolism are zinc-dependent. Zinc plays important roles in growth and development, the immune response, neurological function, and reproduction. On the cellular level, the function of zinc can be divided into three categories: 1) catalytic, 2) structural, and 3) regulatory.

Catalytic role

Nearly 100 different enzymes depend on zinc for their ability to catalyze vital chemical reactions. Zinc-dependent enzymes can be found in all known classes of enzymes.

Structural role

Zinc plays an important role in the structure of proteins and cell membranes. A finger-like structure, known as a zinc finger motif, stabilizes the structure of a number of proteins. For example, copper

provides the catalytic activity for the antioxidant enzyme copper-zinc superoxide dismutase (CuZnSOD), while zinc plays a critical structural role. The structure and function of cell membranes are also affected by zinc. Loss of zinc from biological membranes increases their susceptibility to oxidative damage and impairs their function.

Regulatory role

Zinc finger proteins have been found to regulate gene expression by acting as transcription factors (binding to DNA and influencing the transcription of specific genes). Zinc also plays a role in cell signaling and has been found to influence hormone release and nerve impulse transmission. Recently, zinc has been found to play a role in apoptosis (gene-directed cell death), a critical cellular regulatory process with implications for growth and development, as well as a number of chronic diseases.

Sources of zinc

Zinc is present in a wide variety of foods, particularly in association with protein foods. A vegetarian diet often contains less zinc than a meat based diet and so it is important for vegetarians to eat plenty of foods that are rich in this vital mineral.

Good sources for vegetarians include dairy products, beans and lentils, yeast, nuts, seeds and wholegrain cereals. Pumpkin seeds provide one of the most concentrated vegetarian food sources of zinc.

Benefits of zinc

It plays a crucial role in growth and cell division where it is required for protein and DNA synthesis, in insulin activity, in the metabolism of the ovaries and testes, and in liver function.

As a component of many enzymes, zinc is involved in the metabolism of proteins, carbohydrates, lipids and energy.

It is necessary for a healthy immune system, and is also of use in fighting skin problems such as acne, boils and sore throats.

It is further needed for cell division, and is needed by the tissue of the hair, nails and skin to be in top form.

Zinc is further used in the growth and maintenance of muscles.

Children, for normal growth and sexual development also require zinc.

It also seems as if zinc helps to control the oil glands, and is also required for the synthesis of protein and collagen - which is great for wound healing and a healthy skin.

Deficiency of zinc

There is a shortage of zinc in many people's diet, since zinc is destroyed in the milling process and is also lost in cooking.

Other symptoms of zinc deficiency can include hair loss, diarrhoea, fatigue, delayed wound healing, and decreased growth rate and mental development in infants.

A deficiency will result in an under-performing immune system, open to infections, allergies, night blindness, loss of smell, falling hair, white spots under finger nails, skin problems, sleep disturbances etc.

Men with zinc shortage may have a problem with fertility, while women may experience irregular periods. Children with too little zinc may have stunted growth and slow sexual maturity.

With too little in the body, the sense of smell might suffer, as well as your sense of taste.

Symptoms of high intake

Elevated intake of zinc (1- 2 gram per day) over an extended period can actually harm immune system instead of assisting it. Intake of zinc

should be kept to fewer than 100 mg per day as larger amounts may result in nausea, diarrhea, dizziness, drowsiness and hallucinations.

If one wants to take a zinc supplement, rather take it at night on an empty stomach, as zinc can interfere with the absorption of other minerals such as copper and iron. In a multi-vitamin situation, make sure that the zinc and iron is nearly in the same amounts.

Large intakes of zinc can cause nausea and diarrhea.

When more is needed

Men should always ensure enough zinc in their diets, since the health of their prostate gland is linked to zinc. Zinc is needed to manufacture testosterone and a shortage may induce a low sperm count, loss of libido and other emotional problems. Zinc may also be helpful in fighting infection and inflammation of the prostate gland in older men. It is lost on ejaculation, since sperm needs this mineral to swim towards the egg.

If a women is taking a birth control pill, or receiving hormone replacement therapy, extra zinc may be indicated, and all vegans and vegetarians should also consider their zinc intake, as well as people suffering from psoriasis and women while pregnant or lactating.

People consuming large amounts of alcohol may also be at risk of lowered zinc levels.

Nutrient Interactions

Copper

Taking large quantities of zinc (50 mg/day or more) over a period of weeks can interfere with copper bioavailability. High intake of zinc induces the intestinal synthesis of a copper-binding protein called metallothionein. Metallothionein traps copper within intestinal cells and prevents its systemic absorption. More typical intakes of zinc do

not affect copper absorption and high copper intakes do not affect zinc absorption.

Iron

Supplemental (38-65 mg/day of elemental iron) but not dietary levels of iron may decrease zinc absorption. This interaction is of concern in the management of iron supplementation during pregnancy and lactation and has led some experts to recommend zinc supplementation for pregnant and lactating women taking more than 60 mg/day of elemental iron.

Calcium

High levels of dietary calcium impair zinc absorption in animals, but it is uncertain whether this occurs in humans. One study showed that increasing the calcium intake of postmenopausal women by 890 mg/day in the form of milk or calcium phosphate (total calcium intake, 1,360 mg/day) reduced zinc absorption and zinc balance in postmenopausal women, but increasing the calcium intake of adolescent girls by 1,000 mg/day in the form of calcium citrate malate (total calcium intake, 1,667 mg/day) did not affect zinc absorption or balance. Calcium in combination with phytic acid reduces zinc absorption.

Folic acid

The bioavailability of dietary folate is increased by the action of a zinc-dependent enzyme, suggesting a possible interaction between zinc and folic acid. In the past, some studies found low zinc intake decreased folate absorption, while other studies found folic acid supplementation impaired zinc utilization in individuals with marginal zinc status. However, a more recent study reported that supplementation with a relatively high dose of folic acid (800 mcg /day) for 25 days did not alter zinc status in a group of students being fed low-zinc diets (3.5 mg/day); level of zinc intake did not impair folate utilization in this study.

Vitamin A

Zinc and vitamin A interact in several ways. Zinc is a component of retinol-binding protein, a protein necessary for transporting vitamin A in the blood. Zinc is also required for the enzyme that converts retinol (vitamin A) to retinal. This latter form of vitamin A is necessary for the synthesis of rhodopsin, a protein in the eye that absorbs light and thus is involved in dark adaptation. Zinc deficiency is associated with decreased release of vitamin A from the liver, which may contribute to symptoms of night blindness that are seen with zinc deficiency.

Severe zinc deficiency

Much of what is known about severe zinc deficiency was derived from the study of individuals born with acrodermatitis enteropathica, a genetic disorder resulting from the impaired uptake and transport of zinc. Before the cause of acrodermatitis enteropathica was known, patients typically died in infancy.

The symptoms of severe zinc deficiency include the slowing or cessation of growth and development, delayed sexual maturation, characteristic skin rashes, chronic and severe diarrhea, immune system deficiencies, impaired wound healing, diminished appetite, impaired taste sensation, night blindness, swelling and clouding of the corneas, and behavioral disturbances.

Oral zinc therapy results in the complete remission of symptoms, though it must be maintained indefinitely in individuals with the genetic disorder. Although dietary zinc deficiency is unlikely to cause severe zinc deficiency in individuals without a genetic disorder, zinc malabsorption or conditions of increased zinc loss, such as severe burns or prolonged diarrhea, may also result in severe zinc deficiency.

Mild zinc deficiency

It has recently become apparent that milder zinc deficiency contributes to a number of health problems, especially common in children. The

lack of a sensitive indicator of mild zinc deficiency hinders the scientific study of its health implications. However, controlled trials of moderate zinc supplementation have demonstrated that mild zinc deficiency contributes to impaired physical and neuropsychological development and increased susceptibility to life-threatening infections in young children.

Individuals at risk of zinc deficiency

- Infants and children
- Pregnant and lactating (breast-feeding) women, especially teenagers
- Patients receiving total parenteral nutrition (intravenous feedings)
- Malnourished individuals, including those with protein-energy malnutrition and anorexia nervosa
- Individuals with severe or persistent diarrhea
- Individuals with malabsorption syndromes, including celiac disease and short bowel syndrome
- Individuals with inflammatory bowel disease, including Crohn's disease and ulcerative colitis
- Individuals with alcoholic liver disease who have increased urinary zinc excretion and low liver zinc levels
- Individuals with sickle cell anemia
- Older adults (65 years and older)
- Strict vegetarians: The requirement for dietary zinc may be as much as 50% greater for strict vegetarians whose major food staples are grains and legumes, because high levels of phytic acid in these foods reduce zinc absorption.

The Recommended Dietary Allowance (RDA)

The U.S. recommended dietary allowance (RDA) for zinc is listed by gender and age group in the table below. Infants, children, and pregnant and lactating women are at increased risk of zinc deficiency. Since a sensitive indicator of zinc nutritional status is not readily

available, the RDA for zinc is based on a number of different indicators of zinc nutritional status and represents the daily intake likely to prevent deficiency in nearly all individuals in a specific age and gender group.

Requirements & Recommendations

Zinc: Dietary Reference Intake [1]

	mg/day	Tolerable Upper Intake Levels (UL)
Infants		
0 to 6 months	2*	4
7 to 12 months	3	5
Children		
1 to 3 years	3	7
4 to 8 years	5	12
Males		
9 to 13 years	8	
14 to 18 years	11	23
19+ years	11	34
Females		40
9 to 13 years	8	23
14 to 18 years	9	34
19+ years	8	40
Pregnancy		
< = 18 years	13	34
19 to 50 years	11	40
Lactation		
< = 18 years	14	34
19 to 50 years	12	40

* Value is Adequate Intakes (AI), others are RDA.

The Recommended Dietary Allowance (RDA) for Zinc			
Life Stage	**Age**	**Males (mg/day)**	**Females (mg/day)**
Infants	0-6 months	2 (AI)	2 (AI)
Infants	7-12 months	3	3
Children	1-3 years	3	3
Children	4-8 years	5	5
Children	9-13 years	8	8
Adolescents	14-18 years	11	9
Adults	19 years and older	11	8
Pregnancy	18 years and younger	-	12
Pregnancy	19 years and older	-	11
Breast-feeding	18 years and younger	-	13
Breast-feeding	19 years and older	-	12

Prevention of Diseases or Conditions Related to Zinc Deficiency

Growth retardation

Significant delays in linear growth and weight gain, known as growth retardation or failure to thrive, are common features of mild zinc deficiency in children. In the 1970s and 1980s, several randomized, placebo-controlled studies of zinc supplementation in young children with significant growth delays were conducted in Denver, Colorado. Modest zinc supplementation (5.7 mg/day) resulted in increased growth rates compared to placebo.

More recently, a number of larger studies in developing countries observed similar results with modest zinc supplementation. A meta-analysis of growth data from zinc intervention trials recently confirmed the widespread occurrence of growth-limiting zinc deficiency in young children, especially in developing countries. Although the exact mechanism for the growth-limiting effects of zinc deficiency are not known, recent research indicates that zinc availability affects cell-

signaling systems that coordinate the response to the growth-regulating hormone, insulin-like growth factor-1 (IGF-1).

Delayed neurological and behavioral development in young children

Low maternal zinc nutritional status has been associated with diminished attention in newborn infants and poorer motor function at six months of age. Zinc supplementation has been associated with improved motor development in very low-birth-weight infants, more vigorous activity in Indian infants and toddlers, and more functional activity in Guatemalan infants and toddlers. Additionally, zinc supplementation was associated with better neuro-psychologic functioning (e.g., attention) in Chinese first grade students, but this was observed only when zinc was provided with other micronutrients. Two other studies failed to find an association between zinc supplementation and measures of attention in children diagnosed with growth retardation. Although initial studies suggest that zinc deficiency may depress cognitive development in young children, more controlled research is required to determine the nature of the effect and whether zinc supplementation is beneficial.

Impaired immune system function

Adequate zinc intake is essential in maintaining the integrity of the immune system, and zinc-deficient individuals are known to experience increased susceptibility to a variety of infectious agents.

Increased susceptibility to infectious disease in children

Diarrhea

It is estimated that diarrheal diseases result in the deaths of over 3 million children in developing countries each year. The adverse effects of zinc deficiency on immune system function are likely to increase the susceptibility of children to infectious diarrhea, and persistent diarrhea contributes to zinc deficiency and malnutrition. Recent research indicates that zinc deficiency may also potentiate the effects of toxins produced by

diarrhea-causing bacteria like E. coli. Zinc supplementation in combination with oral rehydration therapy has been shown to significantly reduce the duration and severity of acute and persistent childhood diarrhea and to increase survival in a number of randomized controlled trials. Recently, a meta-analysis of randomized controlled trials concluded that zinc supplementation reduces the frequency, severity, and duration of diarrheal episodes in children less than five years of age. The World Health Organization and the United Nations Children's Fund currently recommend zinc supplementation as part of the treatment for diarrheal diseases in young children.

Pneumonia

Zinc supplementation may also reduce the incidence of lower respiratory infections, such as pneumonia. A pooled analysis of a number of studies in developing countries demonstrated a substantial reduction in the prevalence of pneumonia in children supplemented with zinc. A recent meta-analysis found that zinc supplementation reduced the incidence but not duration of pneumonia or respiratory tract illnesses in children under five years of age.

Malaria

Some studies have indicated that zinc supplementation may reduce the incidence of clinical attacks of malaria in children. A placebo-controlled trial in preschool-aged children in Papua New Guinea found that zinc supplementation reduced the frequency of health center attendance due to *plasmodium falciparum* malaria by 38%. Additionally, the number of malaria episodes accompanied by high blood levels of this malaria-causing parasite was reduced by 68%, suggesting that zinc supplementation may be of benefit in preventing more severe episodes of malaria. However, a 6-month trial in more than 700 West African children did not find the frequency or severity of malaria episodes caused by *P. falciparum* to be different in children supplemented with zinc compared to those given a placebo. Additionally, a randomized controlled trial reported that zinc

supplementation did not benefit preschool-aged children with acute, uncomplicated P. falciparum malaria. Further, a randomized controlled trial in over 42,000 children aged one to 48 months found that zinc supplementation did not significantly reduce mortality associated with malaria and other infections. Due to conflicting reports, it is not yet clear whether zinc supplementation has utility in treating childhood malaria.

Immune response in the elderly

Age-related declines in immune function are similar to those associated with zinc deficiency, and the elderly are vulnerable to mild zinc deficiency. However, the results of zinc supplementation trials on immune function in the elderly have been mixed.

Certain aspects of immune function in the elderly have been found to improve with zinc supplementation. For example, a randomized placebo-controlled study in men and women over 65 years of age found that a zinc supplement of 25 mg/day for three months increased levels of some circulating immune cells (i.e., CD4 T-cells and cytotoxic T-lymphocytes) compared to placebo. However, other studies have reported zinc supplementation does not improve parameters of immune function, indicating that more research is required before any recommendations can be made regarding zinc and immune system response in the elderly.

Pregnancy complications

It has been estimated that 82% of pregnant women worldwide are likely to have inadequate zinc intakes. Poor maternal zinc nutritional status has been associated with a number of adverse outcomes of pregnancy, including low birth weight, premature delivery, labor and delivery complications, and congential anomalies.

However, the results of maternal zinc supplementation trials in the U.S. and developing countries have been mixed. Although some studies have found maternal zinc supplementation increases birth

weight and decreases the likelihood of premature delivery, two placebo-controlled studies in Peruvian and Bangladeshi women found that zinc supplementation did not affect the incidence of low birth weight or premature delivery.

Supplementation studies designed to examine the effect of zinc supplementation on labor and delivery complications have also generated mixed results, though few have been conducted in zinc-deficient populations. A recent systematic review of 17 randomized controlled trials found that zinc supplementation during pregnancy was associated with a 14% reduction in premature deliveries; the lower incidence of preterm births was observed mainly in low-income women. This analysis, however, did not find zinc supplementation to benefit other indicators of maternal or infant health.

Disease Treatment

Common cold

Zinc lozenges

The use of zinc lozenges within 24 hours of the onset of cold symptoms, and continued every 2-3 hours while awake until symptoms resolve, has been advocated for reducing the duration of the common cold. At least ten controlled trials of zinc gluconate lozenges for the treatment of common colds in adults have been published. Five studies found that zinc lozenges reduced the duration of cold symptoms, whereas five studies found no difference between zinc lozenges and placebo lozenges with respect to the duration or severity of cold symptoms. A recent meta-analysis of published randomized controlled trials on the use of zinc gluconate lozenges in colds found that evidence for their effectiveness in reducing the duration of common colds was still lacking.

Two clinical trials examined the effect of zinc acetate lozenges on cold symptoms. While one of the trials found that zinc acetate lozenges (12.8 mg of zinc per lozenge) taken every 2-3 hours while awake

reduced the duration of overall cold symptoms (4.5 vs. 8.1 days) compared to placebo, the other study found that zinc acetate lozenges were no different from placebo in reducing the duration or severity of cold symptoms.

Despite numerous well-controlled trials, the efficacy of zinc lozenges in treating common cold symptoms remains questionable. The physiological basis for a beneficial effect of high-dose zinc supplementation on cold symptoms is not known. Taking zinc lozenges every 2-3 hours while awake often results in daily zinc intakes well above the tolerable upper level of intake (UL) of 40 mg/day. Short-term use of zinc lozenges (e.g., less than five days) has not resulted in serious side effects, though some individuals experienced gastrointestinal disturbances and mouth irritation.

Use of zinc lozenges for prolonged periods (e.g., 6-8 weeks) is likely to result in copper deficiency. For this reason, some experts have recommended that a person who does not show clear evidence of improvement of cold symptoms after 3-5 days of zinc lozenge treatment seek medical evaluation.

Intranasal zinc (zinc nasal gels and nasal sprays)

Intranasal zinc preparations, designed to be applied directly to the nasal epithelium (cells lining the nasal passages), are also marketed as over-the-counter cold remedies. While two placebo-controlled trials found that intranasal zinc gluconate modestly shortened the duration of cold symptoms, three other placebo-controlled studies found intranasal zinc to be of no benefit.

In the most rigorously controlled of these studies, intranasal zinc gluconate did not affect the severity or duration of cold symptoms in volunteers inoculated with rhinovirus, a common cause of colds.

Of serious concern are several case reports of individuals experiencing loss of the sense of smell (anosmia) after using intranasal zinc as a cold

remedy. Since zinc-associated anosmia may be irreversible, intranasal zinc preparations should be avoided.

Age-related macular degeneration

A leading cause of blindness in people over the age of 65 in the U.S. is a degenerative disease of the macula, known as age-related macular degeneration (AMD). The macula is the portion of the retina in the back of the eye involved with central vision. Zinc is hypothesized to play a role in the development of AMD for several reasons:

> (1) Zinc is found at high concentrations in the part of the retina affected by AMD
>
> (2) Retinal zinc content has been shown to decline with age,
>
> (3) The activities of some zinc-dependent retinal enzymes have been shown to decline with age.

However, scientific evidence that zinc intake is associated with the development or progression of AMD is limited. Observational studies have not demonstrated clear associations between dietary zinc intake and the incidence of AMD.

A randomized controlled trial provoked interest when it found that 200 mg/day of zinc sulfate (81 mg/day of elemental zinc) over two years reduced the loss of vision in patients with AMD. However, a later trial using the same dose and duration found no beneficial effect in patients with a more advanced form of AMD in one eye.

A large randomized controlled trial of daily supplementation with antioxidants (500 mg of vitamin C, 400 IU of vitamin E, and 15 mg of beta carotene) and high-dose zinc (80 mg of zinc and 2 mg of copper) found that the antioxidant combination plus high-dose zinc, and high-dose zinc alone, both significantly reduced the risk of advanced

macular degeneration compared to placebo in individuals with signs of moderate to severe macular degeneration in at least one eye.

Data from smaller trials have generally not observed a protective effect of vitamin and mineral supplementation on AMD. At present, there is little evidence that zinc supplementation would be beneficial to people with early signs of macular degeneration, but further randomized controlled trials are warranted.

Diabetes mellitus

Moderate zinc deficiency may be relatively common in individuals with diabetes mellitus. Increased loss of zinc by frequent urination appears to contribute to the marginal zinc nutritional status that has been observed in diabetics. Although zinc supplementation reportedly improves immune function in diabetics, zinc supplementation of 50 mg/day adversely affected control of blood glucose in insulin-dependent (type 1) diabetics in one study.

In a more recent study, supplementation of type 2 diabetics with 30 mg/day of zinc for six months reduced a non-specific measure of oxidative stress (plasma TBARS) without significantly affecting blood glucose control. Presently, the influence of zinc on glucose metabolism requires further study before high-dose zinc supplementation can be advocated for diabetics.

HIV/AIDS

Sufficient zinc is essential in maintaining immune system function and HIV-infected individuals are particularly susceptible to zinc deficiency. In HIV-infected patients, low serum levels of zinc have been associated with a more advanced stage of the disease and also with increased mortality.

In one of the few zinc supplementation studies conducted in AIDS patients, 45 mg/day of zinc for one month resulted in a decreased incidence in opportunistic infections compared to placebo. However,

the HIV virus also requires zinc, and excessive zinc intake may stimulate the progression of HIV infection.

In an observational study of HIV-infected men, increased zinc intake was associated with more rapid disease progression, and any intake of zinc supplements was associated with poorer survival. These results indicate that further research is necessary to determine optimal zinc intakes for HIV-infected individuals.

Sources

Food sources

Shellfish, beef, and other red meats are rich sources of zinc. Nuts and legumes are relatively good plant sources of zinc. Zinc bioavailability (the fraction of zinc retained and used by the body) is relatively high in meat, eggs, and seafood because of the relative absence of compounds that inhibit zinc absorption and the presence of certain amino acids (cysteine and methionine) that improve zinc absorption.

The zinc in whole grain products and plant proteins is less bioavailable due to their relatively high content of phytic acid, a compound that inhibits zinc absorption. The enzymatic action of yeast reduces the level of phytic acid in foods. Therefore, leavened whole grain breads have more bioavailable zinc than unleavened whole grain breads.

Recently, national dietary surveys in the U.S. estimated that the average dietary zinc intake was 9 mg/day for adult women and 13 mg/day for adult men. The zinc content of some relatively zinc-rich foods is listed in milligrams (mg) in the table below.

Food	**Serving**	**Zinc (mg)**
Oysters	6 medium (cooked)	76.3
Crab, Dungeness	3 ounces (cooked)	4.7
Beef	3 ounces* (cooked)	6.0
Pork	3 ounces (cooked)	2.2

Chicken (dark meat)	3 ounces (cooked)	1.8
Turkey (dark meat)	3 ounces (cooked)	3.8
Yogurt, fruit	1 cup (8 ounces)	1.8
Cheese, cheddar	1 ounce	0.9
Milk	1 cup (8 ounces)	1.8
Cashews	1 ounce	1.6
Almonds	1 ounce	1.0
Peanuts	1 ounce	0.9
Beans, baked	1/2 cup	1.8
Chickpeas (garbanzo beans)	1/2 cup	1.3

*A three-ounce serving of meat is about the size of a deck of cards.

Supplements

A number of zinc supplements are available, including zinc acetate, zinc gluconate, zinc picolinate, and zinc sulfate. Zinc picolinate has been promoted as a more absorbable form of zinc, but there are few data to support this idea in humans. Limited work in animals suggests that increased intestinal absorption of zinc picolinate may be offset by increased elimination.

Safety

Toxicity

Acute toxicity

It is generally assumed that zinc is non-toxic because of the strong homeostatic regulation of processes controlling the absorption and secretion of this mineral. However, if zinc is ingested in very high doses it may lead to gastrointestinal distress, abdominal pain, diarrhea, nausea, and vomiting.

Isolated outbreaks of acute zinc toxicity have occurred as a result of the consumption of food or beverages contaminated with zinc released

from galvanized containers. Single doses of 225 to 450 mg of zinc usually induce vomiting.

Milder gastrointestinal distress has been reported at doses of 50 to 150 mg/day of supplemental zinc.

Acute zinc toxicity is rare but has been reported. Outbreaks of acute zinc toxicity have occurred as a result of food and beverage intake contaminated with zinc from galvanized containers, and industrial or accidental exposure.

It can also result in sideroblastic anemia and neutropenia. Ferric iron accumulated in the mitochondria and erythrocyte precursors. Intakes of 2 g or more of zinc sulfate can cause GI irritation.

Other acute toxicity symptoms include metallic taste, nausea, vomiting, lethargy, fatigue, diarrhea, muscle pain and fever.

Chronic zinc toxicity (100-300 mg/d) is more common than acute toxicity and may retard immune function. This type of toxicity occurs from self-supplementation or prolonged use of oral zinc supplements for medicinal purposes.

Excess zinc may also affect copper and iron status and lower plasma HDL concentrations.

Metal fume fever has been reported after the inhalation of zinc oxide fumes. Specifically, profuse sweating, weakness, and rapid breathing may develop within eight hours of zinc oxide inhalation and persist 12-24 hours after exposure is terminated.

Adverse effects

The major consequence of long-term consumption of excessive zinc is copper deficiency. Total zinc intakes of 60 mg/day (50 mg supplemental and 10 mg dietary zinc) have been found to result in signs of copper deficiency. In order to prevent copper deficiency, the

U.S. Food and Nutrition Board set the tolerable upper level of intake (UL) for adults at 40 mg/day, including dietary and supplemental zinc.

Tolerable Upper Intake Level (UL) for Zinc	
Age Group	UL (mg/day)
Infants 0-6 months	4
Infants 7-12 months	5
Children 1-3 years	7
Children 4-8 years	12
Children 9-13 years	23
Adolescents 14-18 years	34
Adults 19 years and older	40

Drug Interactions

Concomitant administration of zinc supplements and certain antibiotics, specifically tetracyclines and quinolones, may decrease absorption of the antibiotic and potentially reduce its efficacy. Taking zinc supplements and these antibiotics at least two hours apart should prevent this interaction.

Additionally, the therapeutic use of metal chelating (binding) agents like penicillamine (used to treat copper overload in Wilson's disease) and diethylenetriamine pentaacetate or DTPA (used to treat iron overload) has resulted in severe zinc deficiency.

Anticonvulsant drugs, especially sodium valproate, may also precipitate zinc deficiency.

Prolonged use of diuretics may increase urinary zinc excretion, resulting in increased loss of zinc.

Further, the tuberculosis medication, ethambutol, has metal chelating properties and has been shown to increase zinc loss.

Linus Pauling Institute Recommendation

The RDA for zinc (8 mg/day for adult women and 11 mg/day for adult men) appears sufficient to prevent deficiency in most individuals, but the lack of sensitive indicators of zinc nutritional status in humans makes it difficult to determine the level of zinc intake most likely to promote optimum health. Following the Linus Pauling Institute recommendation to take a multivitamin/multimineral supplement containing 100% of the daily values (DV) of most nutrients will generally provide 15 mg/day of zinc.

Adults over the age of 65

Although the requirement for zinc is not known to be higher for older adults, their average zinc intake tends to be considerably less than the RDA. A reduced capacity to absorb zinc, increased likelihood of disease states that alter zinc utilization, and increased use of drugs that increase zinc excretion may all contribute to an increased risk of mild zinc deficiency in older adults. Because the consequences of mild zinc deficiency, such as impaired immune system function, are particularly relevant to the health of older adults, they should pay particular attention to maintaining adequate zinc intake.

Zinc excess

Do not get the wrong idea though, zinc is not medication, nor is it something you should avoid. In fact, you should always make sure that your diet includes proper amounts of zinc.

Zinc is an essential mineral that is needed by your body to manufacture about 300 enzymes. Each of these enzymes have diverse processes and functions such as cell reproduction, immunity, protein synthesis, wound repair, vision, free radical protection and immunity.

Zinc Nutrition

Fortunately, a healthy daily diet can provide you with just enough zinc that you need. It is found in ordinary foods that we take such as red

meat, sea foods and poultry. Oysters are the most excellent zinc sources.

If you are not much into meats or seafood, other good sources include beans, whole grains, dairy products, cereals and nuts. However, zinc absorption is more effective if they come from animal proteins than from plant sources.

The Recommended Dietary Allowance of zinc varies, but generally about 9-11 milligrams is enough for adults.

However, the truth of the matter is that only about 30% of the zinc that you intake can get absorbed by your body. Many factors can interfere with zinc absorption such as phytates in your brain and fibers. If your body cannot absorb as much as it needs, you may need to take zinc supplements in order to prevent zinc deficiency.

To date, there is yet a laboratory test that can exactly measure how much zinc your body needs. But if you experience symptoms such as diarrhea, lesions, loss of appetite, growth retardation (in children), hair loss, delays in wound healing, taste abnormalities and so on, your doctor might suspect you to have some form of zinc deficiency. If so, you would most probably be advised to take zinc supplements.

Zinc supplements have also been seen to be effective in shortening cold symptoms, reduce the severity of cold sores, increase energy levels, treat ADHD in children, fighting hair loss and managing conditions such as hypoglycemia and diabetes.

Side Effects of Zinc Supplement

The danger of taking zinc supplements can be summarized in two words: zinc overdose. A zinc dose of 40 milligrams is approved safe to use by FDA and a zinc dosage more than this can pose certain risks.

In terms of zinc toxicity, there is no other way to put it: excess zinc is dangerous!

This is primarily true because too much zinc will likely interfere with the metabolism and absorption of other essential minerals in your body, most especially iron, magnesium and copper.

Zinc side effects can become potentially serious if you take doses from 150 to 450 mg a day. Taking this much can decrease your copper, iron and magnesium levels, reduce your body's immune function, and reduce your HDL (good cholesterol) level.

Zinc Sulfate Side Effects

Oral zinc sulfate supplements can also cause side effects such as stomach upset, heartburn and nausea. Rare side effects have also been reported and these include fever, sore throat, mouth sores, weakness and fatigue.

Zinc is a very important mineral but you only need to take just enough. If you decide on taking mineral supplements for one or more reasons, it is very important that you consult your doctor first and report whatever zinc's side effects you experience.

- Zinc is present in all organs, tissues, fluids and secretions. About 90% of total body zinc is found in skeletal muscle and bone, with much smaller amounts in the liver, gastrointestinal tract, skin, kidney, brain, lung, prostate and other organs.
- The adult human body contains approximately 1.5 to 2.5 grams of zinc.
- In general, about 20% of zinc consumed from a usual mixed diet is absorbed. Unlike other trace elements, zinc does not accumulate in the body to form permanent stores.
- Processing of certain foods may affect amount of zinc content that is available for absorption. Heat treatment may make foods resistant to hydrolysis, by complexing with zinc, making it unavailable for absorption.

- Zinc is primarily an intracellular ion and it functions in association with more than 300 different enzymes of various classes.

Functions

As a component of every living cell in the body, zinc has a multitude of diverse regulatory functions. It is best known for its involvement in enzyme functions and structures:

- Zinc is needed for DNA synthesis, RNA transcription, mitosis, and cell activation.
- Zinc-dependent enzymes are involved in metabolism of proteins, lipids and carbohydrates.
- Zinc plays as essential role in cell membrane integrity.
- Zinc helps manage insulin action and blood glucose concentration.
- Zinc has an essential role in development and maintenance of the body's immune system.
- Zinc is required for bone and teeth mineralization.
- Zinc is involved with normal taste and wound healing.
- Zinc is required for the synthesis of various biological markers of nutrition and of collagen.
- Zinc is essential in regulating gene expression.
- Zinc has long been considered to have anti-inflammatory properties.
- Zinc containing enzymes such as carbonic anhydrase and lactate dehydrogenase are involved in intermediary metabolism during exercise.
- Zinc is particularly important for cells that are rapidly turning over such as those in the immune system; as well as in the maintenance of the central nervous system.

Therapeutic dosages

Therapeutic dosages usually between 5-10 mg of zinc have been used for the treatment of acute diarrhea in infants and children. Therapeutic doses of zinc for the common cold usually range between 10-50 mg of zinc given every 6-8 hours throughout the day. Zinc is usually the preferred therapy to treat Wilson's disease and sickle cell anemia since it has proven to be an effective treatment and is relatively non toxic.

The increasing number of reports that daily supplementation with zinc affects the activities of selective metallo-enzymes along with specific cellular and organ processes, further point out the need to differentiate between meeting the requirements for this nutrient and optimal nutrition.

Deficiency signs and symptoms

- Zinc can be deficient even if plasma levels appear to be 'normal.' A practical criterion is clinical response to zinc supplementation.
- Traditional indicators of zinc status such as plasma levels and measuring activity of zinc metallo-enzymes in blood are relatively resistant to changes in dietary zinc. A good way to measure zinc levels is by looking at granulocytes and lymphocytes because they reflect the body's zinc status fairly accurately. A quantitative assay of alkaline phosphatase activity in the granulocytes is also very useful.
- Numerous factors play a role in zinc deficiency. These include poor dietary zinc intake, excessive dietary phytate intake, chronic illness, malabsorption, or over-supplementation with iron or copper.
- Incidence of zinc deficiency in well-nourished humans is unknown due to difficulties in sufficiently diagnosing zinc deficiency and the diversity of its metabolic roles.
- Among the most sensitive enzymes to dietary zinc intake are deoxythymidine kinase (involved in skin collagen formation) and alkaline phosphatase (involved in the function of granulocytes).
- Symptoms of zinc deficiency include poor growth and development, appetite loss, dermatitis, hypogonadism, alopecia,

reduced taste acuity, delayed wound healing, impaired reproduction and poor immune function.

- Growth retardation and delayed sexual maturation have been some of the most characteristic features of zinc deficiency.
- Clinical zinc deficiency in breastfed infants is accompanied by rashes, dermatitis, failure to thrive, decreased zinc levels in the serum and irritability.
- Severe zinc deficiency is rare and caused by genetic or acquired conditions. Acrodermatitis enteropathica is an autosomal recessive inherited condition of severe zinc deficiency. Symptoms include eczematous skin lesions, alopecia, diarrhea, bacterial and yeast infections, and eventually death if left untreated.
- Moderate deficiency leads to rough skin, poor appetite, mental lethargy, abnormal neurosensory change.
- Mild deficiency symptoms include low testosterone levels, oligospermia, decreased natural killer cell activity, decreased interleukin-2 activity and decreased activity of T helper cells. In addition it may lead to decreased thymulin activity, hyperammonemia, hypogeusia, decreased adaptation to darkness, and a decrease in lean body mass. It is also been suggested that immature B cells accumulate in the spleen in zinc deficiency and as a result lead to enlargement of this organ.
- Other conditions and populations associated with increase risk for zinc deficiency are:

Alcoholism	Trauma	Elderly	Sickle cell anemia	
Stress	Surgery	Lacto vegetarians	Chronic renal disease	Anorexia Nervosa
Malabsorptive syndrome	Geophagia			

Special Needs and Uses

- Zinc requirements are greatest during times of rapid growth such as infancy, adolescence, pregnancy, and lactation. Zinc deficiency affects epidermal, gastrointestinal, central nervous, skeletal, and reproductive systems.

- Adult women are more likely to consume inadequate amounts of zinc. Data reported from NHANES III and CSFII confirm a low dietary intake of zinc for adult women. Results from the Total Diet Study in 1991 indicated that the amounts of zinc provided by the typical diet are below the required daily allowance for children, adolescent females, and women during their reproductive years. The side effects commonly exhibited may include amenorrhea, weight and appetite loss, and skin abnormalities.
- During pregnancy, there are increasing zinc requirements to meet the needs of the mother as well as the developing fetus. Since nutrient stores are deposited during the last three months of pregnancy, a premature fetus is greatly compromised. Zinc is usually the first mineral to be immediately supplemented when it comes to the premature infant. Since zinc is deposited into the body's tissues, low birth weight or intra uterine growth retardation could limit zinc reserves and lead to quick zinc defiency once the child is born.
- Taking a multiple vitamin and mineral supplement with zinc during gestation is one way to ensure a healthy baby. Adverse fetal outcomes associated with maternal zinc status include congenital anomalies, reduced birth weight for gestational age, neural tube defects, and fetal brain function. Maternal complications such as preeclampsia, prolonged labor, and pre-term delivery have also been associated with zinc status. A study conducted in California showed the risk of neural tube defects was associated with increased maternal preconceptional zinc intake. Women who have altered zinc utilization may be advised to take ~25 mg zinc during pregnancy to reduce the risk of complications. However, a study reported that gestational plasma zinc concentrations may not accurately predict pregnancy

outcomes. In addition, more recent studies have shown that a mild zinc deficiency increases maternal morbidity, may result in inefficient labor, and lead to increased bleeding which pose increased risks to the fetus as well.

- Both men and women are at risk for zinc deficiency especially between puberty and the age of 25 due to low dietary intake of zinc as well as increased urinary zinc loss secondary to estrogen and/or stress.
- Zinc deficiency is commonly found in people with eating disorders, malabsorptive syndrome, alcoholic liver disease, chronic renal disease, sickle cell anemia, chronically debilitated individuals, and in those cases when patients present with geophagia.
- Genetic disturbances in zinc metabolism occur in acrodermatitis enteropathica which result in severe zinc deficiency. It is been noted that supplementation with zinc results in increased hedonic tone, motivation, alertness, responsivity, and a decrease in nervousness and restlessness in these patients.
- Patients on TPN may also suffer from zinc deficiency if not adequately replaced since the body loses 6-12 mg of zinc per day. Zinc deficiency can be fatal if left untreated. Common signs of the zinc deficient TPN patient include pustular dermatitis, alopecia, diarrhea, immune dysfunction, weight loss, intercurrent infections due to cell mediated immune dysfunctions and hypogonadism in males.
- Because of Zinc's role in cellular growth it is of particular importance in early childhood as well as for patients needing tissue repair. There is also an increased risk of pneumonia in children with zinc deficiency. Reduced rates of anorexia, cough, diarrhea, fever, and vomiting among zinc supplemented children with stunted growth have also been observed. Studies suggest that zinc may be a more important limiting factor to growth among children in the first two years of life when zinc requirements are higher than compared to older children. Special attention also needs to be placed on children with potential zinc deficiency because, unlike adults, they tend to fail

to adapt to the increased absorption of zinc that happens naturally in adult when there are decreased levels of zinc in the body.

- A significant link between human bone zinc content and bone strength suggests that zinc may play a role in bone health. Although this association has been reported in women, little research on the association between zinc status and osteoporosis in men has been conducted. The purpose of this study was to examine the independent association between dietary zinc and plasma zinc concentration and the association of each with bone mineral density (BMD) and 4 year bone loss in 396 men aged 45-92 years. The research concluded dietary zinc intake and plasma zinc each have a positive association with BMD in men.
- Zinc is a potent mediator of host resistance to infection. This is due to its many roles in basic cellular functions such as DNA replication, RNA transcription, cell division and activation. Numerous animal and human studies indicate that zinc deficiency lowers resistance to infectious diseases. In humans, several studies demonstrated the benefits of zinc supplementation on infectious diseases. Zinc supplementation has been shown to benefit acute and chronic diarrhea and related sickness, acute lower respiratory infections and malaria. Zinc supplementation restored those immunologic indexes associated with sickle cell anemia to near normal. Zinc supplementation normalized certain immune functions and increased resistance to infection in patients with Down's Syndrome. It is suggested that immunodeficiency in the elderly is due in part to zinc deficiency.
- In patients with malignant prostate cancer, high zinc levels which are normally found in normal glandular epithelial tissue, are all greatly reduced by 70-80%. There is no known case where malignant tissue has retained the high zinc or citrate levels which are normally characteristic of healthy prostate tissue. Epidemiological studies have produced contradictory results which have led to the conclusion that the effect of dietary zinc on prostate cancer is complex and possibly confounded by many factors.

- Zinc intake has been associated with decreased risk of distal colon cancer as well as proximal colon cancer. Zinc has been shown to retard the oxidative process possibly by inducing the synthesis of metallothionein a sulfhydryl rich protein that protects against free radicals.
- Recent clinical and experimental findings have reinforced the link among zinc deficiency, malabsorption, and diarrheal disease. It is believed that zinc deficiency makes an organism more susceptible to toxin production by bacteria or enteroviral pathogens that activate guanylate and adenylate cyclases, stimulate chloride secretion, produce diarrhea, and decrease absorption of nutrients further exacerbating an already compromised mineral status. Studies have concluded that zinc deficiency may further decrease the absorption of water and electrolytes and that the gastrointestinal tract is therefore one of the first targets. Zinc has been studied in regards to patients with IBS but results have been contradictory. Zinc is decreased in patients with inflammatory diseases.
- The healing process of gastric ulcers may be enhanced through treatment with zinc, although further studies will be needed to determine to what extent zinc may be beneficial for patients with this condition. Most studies report no or few adverse effects associated with its use.
- There is strong scientific evidence to suggest that zinc may help manage or reduce symptoms of sickle cell anemia. Most of these studies reported increased height, weight, immune system function, and testosterone levels and decreased numbers of crises and sickle cells following zinc treatment.
- Early studies have shown a correlation between low serum free fatty acids and zinc serum levels in children with attention deficit hyperactivity disorder. Additional studies found that zinc supplements reduced hyperactive, impulsive, and impaired socialization symptoms, but did not reduce attention deficiency symptoms. Zinc supplementation may be a more effective treatment for older children with higher body mass index (BMI) scores.

- In several studies, zinc supplements seemed to counteract hypothyroidism and slightly reduce the number of infections in children with Down syndrome. However, zinc did not seem to improve depressed immune systems. Additional human research is needed before a firm conclusion can be made.
- Low-quality studies have been conducted to assess the effects of zinc (topical or taken by mouth) on herpes type I or II. Several of these studies used combination treatments or permitted the continued use of other medications, so the exact role of zinc in those studies is unclear. However, the positive results obtained in most trials suggest that zinc may represent a safe and effective alternative treatment for herpes type I and II and should encourage further research into the topic using well-designed studies.
- Zinc may improve blood cholesterol levels in hemodialysis patients. There is some evidence that zinc may improve cholesterol ratio of HDL 'good cholesterol' versus LDL 'bad cholesterol,' which would be considered a positive effect. Well-designed clinical trials are needed before a strong recommendation can be made.
- Wilson's disease is an inherited disorder of copper metabolism characterized by a failure of the liver to excrete copper, which leads to its accumulation in the liver, brain, cornea, and kidney, with resulting chronic degenerative changes. Early research suggests that zinc treatment may be effective in the management of Wilson's disease. Relatively few cases of adverse effects have been reported, including one case report presenting a fatality; however, it is unclear whether or not the death was caused by zinc. Several studies have been conducted by the same authors, resulting in possible bias. More well-designed trials are needed to confirm these early results.
- Early studies suggest that zinc supplements taken with antibiotics may be more effective than antibiotics alone in reducing pain, urinary symptoms, quality of life, and maximum urethra closure pressure for patients with chronic prostatitis.

- Early studies indicate that daily supplementation with zinc may be of limited usefulness for improving cognition in lead-exposed schoolchildren.
- Early studies of zinc supplements in patients with Crohn's disease have found positive results.
- Diabetic patients typically have significantly lower serum zinc levels compared with healthy controls. In early high-quality studies, zinc supplementation for type-2 diabetics may have beneficial effects in elevating serum zinc level and in improving glycemic control that is shown by decreasing HbA1c concentration.
- Oral zinc supplementation may improve glycemic control and severity of peripheral neuropathy.
- Zinc may reduce the incidence of diaper rash and have a preventative effect.
- Zinc may improve exercise performance in athletes with low serum zinc or zinc deficiencies.
- Gilbert's syndrome is a common, often inherited disorder that affects processing by the liver of the greenish-brown pigments in bile (called bilirubin). The resulting abnormal increase of bilirubin in the bloodstream can lead to yellowing of the skin (jaundice), but the liver itself remains normal. It is more common in men than women and is named after a French gastroenterologist. Zinc sulfate supplementation seemed to decrease serum unconjugated bilirubin levels in a small study.
- Evidence suggests that supplementation with zinc plus iron (but not with zinc alone) may improve linear growth (length) of stunted infants with low hemoglobin.
- Hepatic encephalopathy is abnormal brain function caused by passage of toxic substances from the liver to the blood. Early high-quality trials of zinc for this indication have yielded conflicting results.
- Case report data suggest zinc supplementation may improve thyroid hormone levels (particularly T3) among women with hypothyroidism.

- Many studies report beneficial results of zinc supplements on infertility, as expressed in improved sperm quality and number, although this effect may depend on the cause of infertility. A minor increase in abnormal spermatozoa in subfertile males taking zinc was noted in one study.
- Early studies show potential improvement in uremic patients taking zinc supplements. Zinc supplementation may be recommended only in the patients with proven zinc deficiency, but for all chronic renal failure patients it is questionable.
- Short-term zinc supplementation may increase weight gain and decrease infections, swelling, diarrhea, anorexia, and skin ulcers in children with extreme malnourishment.
- A few studies have examined the efficacy of zinc treatment in leprosy. Studies of zinc taken by mouth report positive results, while one study of topical zinc reports negative results.
- People with alcoholic liver cirrhosis may be deficient in zinc. Preliminary studies suggest that zinc may benefit these patients. The results of one case series suggest that zinc supplementation may improve muscle cramps in patients with cirrhosis.
- Case report data suggest a possible role for zinc supplementation in menstrual cramps.
- . Recent high-quality study data suggest that supplementation with zinc and vitamin A may favorably alter parasites infection rate and duration among children.
- Results from one study show that a combination of spirulina extract plus zinc may be useful for the treatment of chronic arsenic poisoning with melanosis and keratosis.
- There are only a few studies that examine the efficacy of zinc treatment on symptoms of psoriasis, including psoriasis induced arthritis-like symptoms. One trial noted a reduction in pain and joint swelling. Other studies do not support a role for zinc in alleviating the symptoms of psoriasis.
- Radiation has the potential side effect of mucositis, which is inflammation of mucous membranes inside of the mouth, nose, and throat. Two trials suggest that zinc may lower the degree of mucositis in patients on radiation.

- Early evidence suggests that topical zinc oxide oil may help manage perianal and buttock skin damage in incontinent patients.
- A study suggested that supplemental zinc can reverse sexual dysfunction in uremic patients.
- Older adults often have marginal zinc status.
- Individuals totally dependent in IV feedings without added zinc can experience severe zinc deficiency.
- Accumulating evidence supports the hypothesis that magnesium and zinc play significant roles in promoting strength and cardio respiratory function in healthy persons and athletes.

Drug-Mineral Interaction

Zinc requirements are greatest during times of rapid growth such as infancy, adolescence, pregnancy, and lactation.

- Excess zinc can interfere with copper absorption and cause a copper deficiency, which indirectly affects iron status and leads to anemia. Zinc blocks dietary copper but also endogenous copper as well as that in salivary, gastric, and gastrointestinal juices, and so it tends to produce a chronic negative balance. However these characteristics make it an excellent treatment for Wilson's disease in which excessive copper accumulations occur. In the treatment of Wilson's disease the dose given is usually 50 mg of elemental zinc (as acetate) 3 times a day given in a fasting or post-absorptive state. It is relatively non-toxic and only about 10% of patients on this therapy complain of stomach upset which is relieved by taking zinc only in the post-absorptive state instead of the fasting state.
- In the treatment of patients with sickle cell anemia, zinc supplements have been found to induce hypocupraemia and associated neutropenia and microcytosis. This condition can be corrected by administration of copper.
- Excess copper intake, calcium, dietary fiber, or iron supplements can decrease absorption of zinc. Intake of iron supplements should be separated from zinc-containing supplements.

- Zinc interferes with folate absorption.
- Many minerals, including zinc, may interfere with absorption of fluoroquinolone antibiotics, such as lomefloxacin, and tetracyclines, such as doxycycline. To prevent this interaction problem, take mineral supplements far apart from antibiotic intake.
- Angiotensin-converting enzyme (ACE) inhibitors may cause zinc depletion.
- Zidovudine, an antiviral agent used to treat HIV infection, may deplete plasma concentrations of many minerals, including zinc.
- Orlistat or any medication which can result in steatorrhea or malabsorption can lead to poor absorption of zinc and possibly deficiency.
- The use of some chelating agents, such as penicillamine is used in the treatment Wilson's disease and other various chronic debilitating illnesses may also lead to zinc deficiency.
- More research is needed to assess the bioavailability of different zinc compounds used in supplements. However, looking at a meta-analysis of 25 clinical trials including compounds such as zinc sulfate, zinc acetate, zinc gluconate, zinc methionine, zinc carbonate and zinc oxide it is reasonable to conclude that zinc acetate and zinc sulfate are fairly similar in terms of bioavailability, and that zinc oxide and zinc carbonate are usually poorly absorbed. However this meta-analysis is limited by the amount of data available. Most data available involves either zinc sulfate or zinc acetate. In addition, when investigating how the source of zinc was decided for each trial scientists stated that they were limited to only using compounds which the subjects found palatable. Apparently zinc sulfate has an acceptable taste in doses of 15-50 mg if mixed with citric foods such as orange juice.

Selected Food Sources of Zinc

Food	Milligrams (mg) per serving	Percent DV*
Oysters, 6 medium	76.7	513
Beef shanks, cooked, 3 ounces	8.9	59
Crab, Alaska king, cooked, 3 ounces	6.5	43
Pork shoulder, cooked, 3 ounces	4.2	28
Breakfast cereal fortified with 25% of the DV for zinc, ¾ cup serving	3.8	25
Chicken leg, roasted, 1 leg	2.7	18
Pork tenderloin, cooked, 3 ounces	2.5	17
Lobster, cooked, 3 ounces	2.5	17
Baked beans, canned, ½ cup	1.7	11
Cashews, dry roasted, 1 ounce	1.6	11
Yogurt, fruit, low fat, 1 cup	1.6	11
Raisin bran, ¾ cup	1.3	9
Chickpeas, ½ cup	1.3	9
Cheese, Swiss, 1 ounce	1.1	7
Almonds, dry roasted, 1 ounce	1.0	7
Milk, 1 cup	0.9	6
Chicken breast, roasted, ½ breast with skin removed	0.9	6
Cheese, cheddar or mozzarella, 1 ounce	0.9	6
Kidney beans, cooked, ½ cup	0.8	5
Peas, boiled, ½ cup	0.8	5
Oatmeal, instant, 1 packet	0.8	5
Flounder or sole, cooked, 3 ounces	0.5	3

* DV = Daily Value. DVs were developed by the U.S. Food and Drug Administration to help consumers compare the nutrient contents of products within the context of a total diet. The DV for zinc is 15 mg for adults and children age 4 and older. Food labels, however, are not required to list zinc content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient.

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Interactions with Herbs and Dietary Supplements

Zinc may interact with LDL, HDL lipoproteins, and triglycerides, reducing HDL "good" cholesterol levels. Use cautiously with herbs and supplements taken for cholesterol, due to possible additive effects.

Zinc may interfere with copper metabolism. However, one study indicates no detrimental effects of zinc on plasma copper levels in healthy volunteers over a period of six weeks.

Non-heme iron may decrease zinc absorption. Non-heme iron and zinc compete for a common absorption pathway in the gut. However, when iron and zinc are taken with food, this interaction is not likely to occur. When taken with food, zinc absorption is facilitated by proteins in food through an alternate pathway that does not compete with iron. Protein-bound heme iron (found in red meats) does not seem to affect zinc absorption.

Zinc supplementation has been shown to alter thyroid hormone metabolism in disabled patients with zinc deficiency.

Zinc may interact with herbs and supplements that contain caffeine or have blood pressure-altering, antibiotic, hormonal, diabetic, hypoglycemic, or diuretic effects.