BEEF FACTS: Nutrition

Zinc and Immune Response

Zinc, an essential trace element, rich in meat such as beef and other animal products, plays a critical role in immunity (1-4). Individuals with adequate zinc status are better able to fight infections caused by viruses, bacteria, and parasites than are individuals with suboptimal zinc status (1). Even mild or moderate zinc deficiency can weaken immune systems (1, 4). Low plasma zinc levels characterize a variety of congenital and acquired diseases associated with impaired immune response (1). Fortunately, increasing zinc intake corrects immunological disorders related to zinc deficiency (1-4).

The Body's Immune System

Studies in both experimental animals and humans indicate that zinc affects numerous aspects of the body's immune system ranging from the barrier of the skin to gene regulation within white blood cells (1, 4). The body protects itself from potentially harmful microorganisms such as bacteria, viruses, and fungi by both *nonspecific* and *specific* defense mechanisms.

Phagocytosis, the process by which certain cells (e.g., macrophages) recognize, engulf, and destroy antigens (i.e., toxins, foreign proteins, or bacteria) is a *nonspecific* immune defense mechanism in which zinc is involved. Zinc also influences nonspecific immunity by its effect on neutrophils and natural killer cell activity (4).

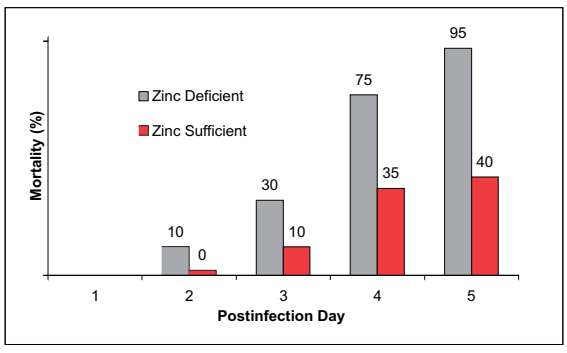
Zinc plays an important role in *specific* immune defenses such as **humoral** and **cell-mediated** immunity (1). The **humoral** immune response relies on the production of proteins, called antibodies or immunoglobulins, by a type of white blood cell (B-lymphocytes). A deficiency of these white cells is associated with bacterial (e.g., cholera) and viral (e.g., measles) infections. Following a complex process of recognizing antigens, B-lymphocyte cells multiply and produce antibodies that bind and destroy antigens.

Cell-mediated immunity, on the other hand, relies on another type of white blood cell, called T-lymphocytes which mature in the thymus gland. These special cells, together with specialized proteins, destroy specific microbes or abnormal cells (1,4,5). In the process, some T-lymphocytes, like some B-lymphocytes, retain a "memory" of the invading microbe (bacteria, viruses, fungi) with the result that such microbes can be dealt with more quickly should they reappear in the future. A deficiency of T-lymphocytes is associated with many viral (e.g., herpes simplex) and some bacterial (e.g., tuberculosis) and fungal (e.g., candidiasis) infections. Zinc is required for the activation of thymulin, a hormone that stimulates the development of white blood cells into T-lymphocytes with specific functions (e.g., "helper," "suppressor," and "killer" T cells) (2).

Zinc Deficiency Impairs Immune Function in Experimental Animals

Zinc deficiency causes marked changes in the immune system in a variety of animal species, evidenced by the increased mortality and morbidity of zinc-deficient animals challenged with bacteria, viruses, and parasites (1,4). In mice fed a low zinc diet for 30 days, 30% to 80% losses in immune defense capacity occurred (1). Zinc-deficient animals exposed to infectious agents such as *Listeria monocytogenes* are more likely to die or die earlier than zinc-sufficient animals (Figure 1) (1,5).

Figure 1. Zinc Status Influences Mortality in Mice Infected with *Listeria monocytogenes*[1]



[1] Adapted from Chandra, R.K. (5).

Low zinc intake in experimental animals adversely affects the lymphatic system which fights infections. The weight of lymphoid organs such as the thymus and spleen and the number of T-lymphocytes are reduced in zinc-deficient animals (1). Even in mild zinc-deficiency, T cell number may be decreased and blood levels of immunoglobulins may be reduced (6).

The decrease in immune response in zinc deficient animals appears to result from a reduction in the number of lymphocytes and not from a change in the host defense capacity of the remaining lymphocytes (7). Residual lymphocytes of zinc deficient animals are able to initiate immune responses (7). Abnormalities in cell-mediated and humoral immunity in zinc-deficient animals can be reversed by zinc repletion.

Zinc deficiency in experimental animals also interferes with nonspecific immune defense mechanisms such as phagocytosis. In zinc-deficient animals infected with pathogenic parasites, the function of macrophages (i.e., large cells that engulf bacteria and other foreign matter) is impaired. However, phagocytosis can be restored to normal when the animals receive sufficient zinc (1,8,9).

Zinc Deficiency Impairs Immune Function in Humans

Immune dysfunctions in zinc-deficient humans are similar to those described in zinc-deficient animals. In humans with low zinc status, risk of infectious diseases increases (4). Various congenital and acquired diseases associated with impaired immune response are characterized by low plasma zinc levels (1). Early evidence of zinc's role in immune functions was provided by findings in patients with acrodermatitis enteropathica, a rare genetic disorder characterized by partial inability to absorb zinc (1,4,10). Patients with this disease are marginally to severely zinc deficient, and have a high incidence of serious infections of the skin and mucosa, as well as abnormalities in immune responses (10). For example, there are reductions in the activity of the hormone thymulin, in the production of lymphocytes, and in delayed type hypersensitivity responses (10). Early correction of zinc deficiency in these patients restores immune function and eliminates infection (10).

Immunological defects associated with zinc deficiency have been described in patients receiving total parenteral nutrition without adequate zinc, in children with protein-calorie malnutrition or marasmus, and in patients with secondary zinc deficiency (1,4). Secondary zinc deficiency can result from gastrointestinal disorders, human immunodeficiency virus (HIV), sickle cell anemia, renal disease, some types of cancer, and alcoholism (1,4).

When low birth weight full-term infants in Brazil were given 5 mg zinc/day for 8 weeks, diarrhea and cough decreased and immune function improved (11). Other studies in zinc deficient children in developing countries have shown that zinc supplementation reduces the incidence, duration, and severity of diarrhea, as well as acute lower respiratory infection (12). HIV-infected individuals are particularly susceptible to zinc deficiency and increased zinc intake may diminish immune defects associated with this disease, thereby inhibiting progression of the disease and enhancing resistance to other infections (13,14). However, supplementation with zinc must be carried out with caution because excess zinc may stimulate HIV (13).

Although zinc supplementation, particularly in the form of zinc lozenges, has been suggested to prevent or at least shorten the duration of colds, the evidence is conflicting (1,15,16). Additional support for zinc's role in immunity is provided by findings of low blood levels of thymulin in mildly zinc-deficient adults and restoration to normal levels with zinc repletion (1).

Can Zinc Restore Immune Function in Older Adults?

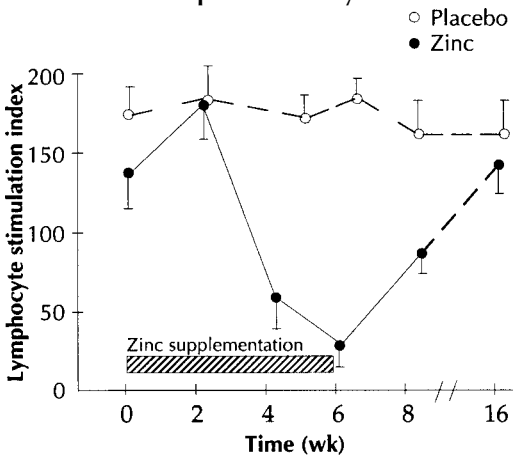
Inadequate intake of zinc may contribute in part to the weakened immune system and increased susceptibility to infection and disease in many older adults (13,14,17). Advancing age is accompanied by changes in immune function, such as a decline in immune responses, particularly cell-mediated immunity, which are similar to those that occur with zinc deficiency (17).

An adequate intake of zinc is particularly important for older adults, many of whom are at risk for zinc deficiency. However, the evidence is inconclusive as to whether increased zinc enhances immune function, especially in individuals who are not zinc deficient, or reverses the age-related decline in immunocompetence (13).

Too Much Zinc Reduces the Body's Ability to Fight Infection

Studies in experimental animals and humans indicate that extreme excesses of zinc can suppress the immune system (18,19). In 11 healthy young men, supplementation with 300 mg of zinc a day, or about 30 times the current Recommended Dietary Allowance (RDA) of 11 and 8 mg/day for males and females, respectively (19), reduced several immune functions, including stimulation of lymphocytes (18, Figure 2). Al-

Figure 2. Excess Zinc Impairs Immunity.[1]



[1] Reproduced, with permission, from Chandra (18). Copyright 1984, American Medical Association.

though zinc is relatively nontoxic, chronic intake of this trace element in excess of recommended amounts is not advised without close medical supervision. It is difficult to consume excess zinc without taking zinc supplements. The Tolerable Upper Intake Level (UL), or the highest level of daily zinc intake unlikely to pose adverse health effects for most individuals, is 40 mg/day for adults 19 years and older (19).

How Zinc Regulates Immunity

Exactly how zinc influences the immune response is unknown, although several possibilities have been proposed (1,4). These include zinc's role in maintaining the biological activity of the hormone, thymulin, or in regulating genetic expression for differentiation and proliferation of cells involved in immunity. Zinc also has a role in normal cellular replication and growth which can affect the rapidly proliferating cells of the immune system. In addition, zinc is required as a co-factor for numerous metalloenzymes involved in the continuous production of cells of the immune system. Zinc may also modulate apoptosis or cell death which has a key role in immune integrity (1).

Meeting Zinc Needs

Zinc deficiency can result from consuming a diet low in zinc and/or from conditions that increase the body's need for zinc, reduce zinc absorption, or exacerbate zinc loss. Chronic infection, cancer, or surgery can increase the body's requirement for zinc. Other conditions such as gastrointestinal dysfunction or chronic inflammatory bowel disease can decrease the body's absorption of zinc. Renal disease, diabetes mellitus, alcoholism, or the use of certain medications promote zinc loss.

Considering that zinc deficiency, even if mild, compromises immune function and increases susceptibility to a variety of infectious diseases, it is important to meet zinc needs (Table 1). Both the zinc content of food and its bioavailability influence zinc status (20). Animal products such as meat (especially beef), poultry, seafood (especially oysters), and dairy foods are the best food sources of zinc. In fact, beef is the primary dietary source of zinc for U.S. children and adults (21,22). Cereals, grain products, fruits, and vegetables also contain zinc, although in smaller amounts than in animal products. In addition, zinc is more readily absorbed from animal, than from vegetable, sources (20). For the above reasons, it is important to consume the recommended two to three servings of foods from the Meat Group each day to meet zinc needs and to protect against infectious diseases.

Table 1. Recommended Dietary Allowances (RDAs) for Zinc[1]

Population	Age (yr)	Zinc (mg/day) Male	Female
Infants	0.7 – 1.0	3	3
Children	1 – 3	3	3
	4 – 8	5	5
	9 – 13	8	8
	14 – 18	11	9
Adults	19 – 50	11	8
	> 51	11	8
Pregnant Women	≤ 18		13
	19 – 50		11
Lactating Women	≤ 18		14
	19 – 50		12

[1]Adapted from Institute of Medicine, Food and Nutrition Board (19).

Summary

Zinc is essential for the normal development and maintenance of immune functions. Nutritional zinc deficiency and immunodeficiencies are encountered in a number of patients with a variety of diseases. Both deficiencies and extreme excesses of zinc can impair immunity or the body's ability to fight infection. However, it is difficult to consume excess zinc without taking zinc supplements. Nutritionists recommend consuming a variety of foods from the basic food groups each day to meet zinc needs. An adequate intake of bioavailable zinc from dietary sources such as animal products (e.g., meat such as beef) is beneficial to immune function and overall good health.

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For more information, contact:

Nutrition Research
National Cattlemen's Beef Association
P.O. Box 670
Bloomingdale, IL 60108-0670
(800) 368-3138
www.beefnutrition.org

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