Zinc and Immune Function
The Importance of Zinc for Health
Susanna Cunningham-Rundles
History

The crucial significance of zinc for human growth and development has gradually emerged over the last three decades. Investigations of human nutritional status have shown that zinc is not as freely available as the ubiquitous distribution of this trace element might suggest. Furthermore, a number of clinical studies have revealed that the effects of even a moderate degree of zinc deficiency may be profound. Zinc was initially found to be an essential element for the growth of plants and animals more than 100 years ago when scientists were seeking to discover the basic requirements for growth, and deliberately reduced or eliminated zinc from the food of plants, microbes, and animals. In all cases, growth was radically reduced, and in some experiments the effects were lethal. Although these studies attracted much attention for their basic significance, it was assumed that implications for human health were minimal, since zinc was thought to be widely available in nature. However, in the 1960’s, this view suddenly changed, when human zinc deficiency was reported for the first time and a new field opened up.

As often happens in science, there was a synchronicity and a convergence among discoveries that included the appearance of a new science called “immunology” at the same time that evolving studies in the ancient science of nutrition were illuminating the essential relationship between poor nutrition and susceptibility to infection. A central figure in these studies was Dr. Ananda Prasad, a hematologist working in Iran, who found that low zinc levels in blood were causally related to a rare condition of dwarfism, testicular retardation, and susceptibility to infections in a group of patients who, although not genetically related, were alike in having a diet that produced zinc deficiency (1). This diet, consisting only of bread and clay, was both low in zinc and contained phytic acid, which was subsequently discovered to form complexes with zinc which could interfere with absorption from the gastrointestinal tract. We now know that the absorption of zinc takes place primarily in the small intestine and that both ingested dietary components and those produced during digestion may either facilitate or impair zinc uptake.

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HOW ZINC AFFECTS IMMUNE FUNCTION

- Zinc is a structural component of thymic hormone
- Zinc is a lymphocyte mitogen (causes expansion of immune cells)
- Zinc regulates immune function
The possibility that major disease might be solely caused by a block in zinc absorption was subsequently confirmed by the discovery of a genetically transmitted lethal mutation in Holstein-Fresian cattle. Curiously, a major immune organ, the thymus gland, was found to be shrunken in these cattle, suggesting a possible explanation of why the cattle died from infections.

Very soon after, a new human genetic condition called human Acrodermatitis enteropathica was described. Infants born with this condition developed skin lesions, serious diarrhea, hair loss, and became very sick. Faulty zinc absorption rapidly lead to immune deficiency and to the development of life threatening infections (2). Amazingly, all of these symptoms could be resolved by giving intravenous zinc to replete zinc stores (3). Again, the chief physical organ affected in these babies was the thymus.

The thymus was known as a “barometer of nutrition” because children dying from infections associated with protein calorie malnutrition were found to have little thymic tissue. The thymus gland was already known to be very important in the development of the immune system. After birth, all of the cells of the immune system appear first in the bone marrow. Those that will have the capacity to recognize “self” from “non self” and therefore can recognize potentially infectious microbes, must ultimately develop, or as it is sometimes termed, be “educated”, in the thymus. These cells called “precursor” cells of the immune system arise in the bone marrow and, after circulating through the thymus, emerge as active “Thymus- cells”, or “T” cells as they are called. Since zinc is essential for the growth and development of all cells, it was not surprising that the babies with low zinc had poor thymic development. This led to reduced and weak T cells which were not able to recognize and fight off certain infections. The implications of this thymic atrophy induced by zinc deficiency was studied further by Dr. Robert A Good and his colleagues. When they and others found that either zinc administration or T cell infusions could prevent infections and reverse lethality in zinc deficient mice (4,5), the importance of the immune system as a critical target of zinc deficiency was proven.

Current View of Zinc and Immunity

In the years since the original discovery of how zinc influences the immune system, many groups have studied zinc (6) and other links between nutrition and immunity. Indeed there is growing evidence that nutrients have actually evolved as co-factors in development and maintenance of immune response (7) and that nutrients directly affect both immediate and long term defense against infections and even susceptibility to certain tumors. The course of infections as diverse as measles and HIV may be directly affected by nutrient deficiency.
In all of these studies, including those involving the entire range of essential micronutrients, both vitamins and minerals, zinc continues to show the most specific and in many ways the strongest effect on the function of the immune system of any micronutrient. Zinc has a unique role in thymus dependent "T" cell mediated immune response. In addition to combining with thymic hormone to form the biologically active thymic hormone molecule (8), even a mild reduction of circulating zinc levels is associated with reduced T cell production of certain critical proteins called cytokines which regulate immune response and act as growth factors for the immune system.

Now, as a result of much research, zinc is included in human nutrient solutions and infant formulas. The benefit of normal levels of zinc on immune response is clear and the use of supplements to achieve this is well established. Since zinc competes with copper for uptake from the gastrointestinal tract, over-supplementation can occur with indiscriminate use and may even lead to low copper levels, which can have deleterious effects on the cardiovascular system. However, while the value of a balanced diet cannot be overestimated in providing a true basis for health, zinc supplements in moderation can be helpful in maintaining normal zinc levels.

In summary, the critical nature of zinc interaction with T cells in the development of defense against potential pathogens continues to be at the cutting edge of current research on how nutrients affect immune response. These studies show that zinc is essential for normal human immune function.

References