

Nutrition and Aging: Supporting the Aging Immune System

David Barnes PhD, Director of Research, Standard Process Inc.

The immune system is an incredibly complex “organ” and it is the focus of many articles and books. Space constraints require we take a brief and superficial look at the relationship between nutrition and the functioning of the immune system, particularly during aging. It is well recognized that the protein/energy malnourished individual is often immunocompromised (7). What is not fully understood is the relationship between supplementation to alleviate modest nutrient deficiencies and corresponding improvement in immune function. The first section of this article provides an overview of the immune system, with emphasis on aging, and is followed by a discussion of what is known about the role various nutrients play in immune function.

The immune system is designed to recognize and protect against substances and organism (antigens) that are foreign and potentially harmful to the body. The immune system must also be able to distinguish foreign antigens from self. The immune system is made up of two parts, *innate* or cell-mediated immunity and *humoral* or adaptive immunity. The innate immune system is designed for rapid defense. The humoral immune system provides long-term coordinated protection against future repeat exposure to antigens (15).

Innate immunity is provided by barrier tissues such as the skin, respiratory tract, and intestinal membranes working in conjunction with chemical secretions (mucous) and cellular components (phagocytic and secretory cells). The innate immune system can draw upon a variety of cells to provide protection, including neutrophils, macrophages, mast cells, eosinophils, and natural

killer cells – all functioning to recognize and destroy foreign invaders. The physiological responses of these cells are controlled by numerous regulatory molecules including prostaglandins, leukotrienes, major histocompatibility complex molecules, immunoglobulins, and chemokines. This list is by no means comprehensive but provides a picture of the complexity of the immune system and illustrates the difficulties in understanding the role of nutrition in its function (15).

When the innate immune system is overwhelmed by harmful antigens or is weakened by infection, the humoral immune system responds as the next level of protection. Humoral immunity is largely the responsibility of circulating T and B lymphocytes that are regulated by secreted proteins called cytokines. T and B cells work together to produce a coordinated cell- and antibody-mediated response to antigens. This type of immunity has a memory and often responds later in life to combat repeat exposure to antigens or infections. However, as we age this immune memory can slowly fade (15).

The innate and humoral immune systems combine to form a powerful tool for protection against infection. As people age, the immune system, like most other organs and tissues, loses some function. The degree of dysfunction is determined by many factors, some genetic and many environmental. Diet and nutrition is a modifiable environmental factor that can influence and improve immune function during the normal aging process.

Aging

Aging can be described as the result of progressive deterioration of many physiological functions potentially leading to dysfunction and disease. Indeed, some experts theorize that aging is actually due to changes within the immune system leading to less surveillance and protection against harmful antigens and microorganisms that cause disease. It has been further suggested that the age-related decline in immune function is due to nutritional deficiencies or increased nutritional requirements not being met. Taking it a step further, the question is raised whether appropriate nutrient supplementation can improve immune function during aging and thereby decrease the risk of disease (3).

Certainly a well maintained immune system contributes to longevity. Changes in the immune system with age are separated into *primary*, normal age-dependent decline in immune function, and *secondary*, decline in immune function due to environmental factors. Age-dependent changes include decreases in hormones regulating the thymus, leukocyte function, antibody responses, delayed type hypersensitivity, and lymphocyte proliferation. Environmental factors include exposures to toxic chemicals and harmful microorganisms as well as deficiencies in nutrients required for proper immune function. Obviously, such deficiencies could have an impact on age-dependent changes in the immune system. In addition, aging is often associated with decreased absorption and metabolism of nutrients that can lead to deficiencies.

Nutrition and Immunity

The strongest links between nutrition and immune function are found with a select few nutrients including retinol, pyridoxine, ascorbic acid, vitamin B12, folate, vitamin D, and the minerals

iron, zinc, copper, and selenium (1). In general, cell mediated immunity is more sensitive to micronutrient deficiencies than humoral immunity (3). The importance of maintaining a healthy intake of these and other nutrients is illustrated most strikingly in the combination of modest nutrient deficiency and compromised immune function. Where the two overlap there are often negative synergistic effects – a greater impact on health than with either physiological state alone (12). Poor nutrition compromises the ability of the immune system to function effectively but at the same time the action of the immune system can lead to poor nutrition. This occurs due to reduced intake of essential nutrients during an infection, due to reduced nutrient absorption or due to increased requirements. In addition infections can cause nutrient redistribution independent of nutrient status. During some infections, plasma levels of copper increase while plasma retinol, iron, and zinc decline.

Nutrients and Immune Function

Zinc

Zinc deficiency is widespread in most populations, but even marginal zinc deficiency has marked effects on immune function resulting in higher incidence of microbial infections (10). This mineral is prevalent in many key enzyme systems used by the immune system and thus zinc insufficiency will impact both the innate and adaptive immune systems. Preventive zinc supplementation has been shown to decrease the severity of rhinovirus infections (9,13).

Iron

Plasma levels of iron decline during an infection. This sequestration may be an attempt to limit the growth of microbes that require this mineral. Similar to zinc, dietary iron insufficiency can

have a significant impact on immunity since many of the enzymes used in the immune response contain iron for their function.

Copper

Plasma levels of copper increase during infection. This is in part due to the production of ceruloplasmin, an important copper-dependent protein produced during the acute phase response to infection. Ceruloplasmin has ferroxidase activity which aids iron sequestration.

Retinol

Retinol, or vitamin A, plays a central role in the maintenance of epithelial tissues such as those in the respiratory and gastrointestinal tract (barrier tissues). The reduction in plasma vitamin A observed during infection may be a defense mechanism to help maintain body vitamin A stores. Infection causes a decrease in the production of retinol binding protein required to transport vitamin A around the body. As a result, supplementation during an infection may be far less effective than supplementation *prior* to the infection (preventive) since the vitamin won't be able to get to where it is needed during the infection.

Ascorbic Acid

Plasma and cellular levels of ascorbic acid, an important antioxidant, decline with infection, though it is not clear if this is a normal protective response. Its antioxidant action may be an important protective mechanism for cells of the immune system as they attack and kill offending microbes (known as the "respiratory burst"). It is interesting to note that the dose of this nutrient can cause differential effects. For example high levels of ascorbic acid (600 – 1000 mg) inhibit

the immune response, whereas low ascorbic acid (200 mg) enhances function. As a result, “mega-doses” of vitamin C may not be beneficial (3).

Nutritional Supplements and Immune Function

There are relatively few studies examining nutritional supplementation and immune function in people and many of the ones that have been conducted have been criticized for some weakness or another. The major research limitation in this area is the sheer complexity of the immune system and the cost required to study many biomarkers in a large population. In addition, it is not always clear what parameters of immune function are valid to measure. Where research has been conducted, the interventions tend to be large doses of single nutrients or multivitamins as opposed to complex dietary factors. Despite this, it is reasonable to conclude supplementation can improve immune function and thereby health. For example, Santos et al. (1996) showed that retinol supplementation was associated with increased natural killer (NK) cell activity. Similar observations were made with beta-carotene (16). Goodwin and Garry (1983), on the other hand, examined immune function in health elderly subjects consuming vitamin and mineral supplements and found that high levels of supplementation had no apparent impact on immune function. The follow-up research led them to suggest that in the absence of an immune challenge, one might not expect to see large changes in biomarkers of function.

It is interesting to note that where dose has been examined there is evidence of synergy among micronutrients and a greater benefit with lower levels of supplementation (4,5). Bogden and Louria (2004) concluded that high doses of single nutrients may improve immune function but

the effects do not seem to persist and depending on the nutrient may interfere with the beneficial effects of other nutrients (negative synergy). Length of supplementation also impacts outcome and can lead to inappropriate conclusions about the value of supplementation. This is because nutritional determinants of immune function tend to act over long time periods. As a result, short-term studies (days/months) tend to be highly variable in their outcomes whereas long-term supplementation studies (years) consistently show positive effects.

Any discussion of immune function and diet cannot be complete without a mention of probiotics, particularly with regard to the elderly. The balance of microbial populations in the gastrointestinal tract can have a significant impact on the immune function since the gut is heavily monitored by cells of the immune system. The mucosal immune response to new antigens is diminished in aging (6). Of the many attributes associated with consumption of probiotics is a beneficial role in immune-based diseases. The mechanism of probiotic action is unclear and this may explain their limited use. However, certain strains of microflora show clear effects on immune enhancement. Evidence suggests that probiotics have an immune modulating role in allergic responses in the gastrointestinal tract, inflammatory bowel disease, Crohn's disease, diabetes, and rheumatoid arthritis. Many of these ailments are prevalent in elderly people. Probiotics also have been studied as a preventative and treatment for antibiotic and microbial induced diarrhea.

In recent years, more interest is being placed on the synergistic effects of multiple nutrients and the advantages of strengthening the relationship between specific nutrients and immune function (2,11). Supplements are being designed to exploit beneficial interactions between nutrients in

relation to immune function. Indeed with the coming of personalized medicine one might envision nutrient combinations designed to be patient- and condition-specific. The complexity of nutrition/immune function interrelationships requires significantly more research to be conducted.

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