



What Is the Strength of the Evidence for Supplement Use for a Healthy Immune System?

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Both genetic and environmental factors are known to cause a decline of the immune system during aging.¹ Attempts to prevent the loss of genome integrity and damage to cellular DNA in immune cells during aging are of vital importance. With age, cumulative damage caused by both exogenous and endogenous agents such as UV or ionizing radiation, and reactive oxygen species generated by respiration could further increase the damage to DNA, resulting in the impairment of immune function. Loss of various immunological functions in the elderly includes both changes in innate (rapid) and adaptive (delayed) immune responses, which are regulated closely by various lymphocyte subsets. With age, the loss of T-cell function, particularly changes in the naïve/memory T-cell ratio, occurs earlier than the loss of B cell function, which causes an imbalance in Th-1 (IL-2, IFN- γ) and Th-2 (IL-4, IL-6, IL-10) cytokines.² These changes may promote either organ specific or systemic inflammation and an increase in autoimmune disorders in the elderly, including susceptibility to viral and bacterial infection. Inadequate nutrition and/or selective dietary deficiency in the elderly also could cause immune deficiency. Furthermore, early loss of immune function may lead to failure to ward off diseases of aging such as cardiovascular disease, cancer, and various autoimmune disorders such as arthritis and osteoporosis. Thus, there is a growing interest among the elderly population in the regular use of various dietary supplements (DS) to restore declining immune function to prevent infection and diseases of aging. This presentation will review briefly a few commonly consumed DS presently used by many of the elderly to restore immunity and vitality such as vitamin E (vit E), zinc, n-3 fatty acids (fish oil), and native American cone flower or Echinacea.

Echinacea: Echinacea is a native plant used by Native Americans. Indirect evidence suggests that a soluble root extract from the Echinacea plant may possess anti-inflammatory and/or anti-viral properties and may be effective against cold and flu symptoms.^{3,4,5,6} Both animal and human studies showed some positive as well as negative results. Some reports indicate that it acts as an immuno-stimulatory agent by increasing the production of pro-inflammatory cytokines (IL-1, IL-6, and TNF- α). Because of many uncertainties from several animal and human studies, it may be useful to undertake, initially, a few animal studies with well-defined Echinacea products to measure its immuno-stimulatory properties on various cellular and humoral immune responses. This includes expression of various gene products in various target tissues and/or immune cells to determine the future need for human studies.

Vitamin E: Vitamin E has been recognized for several years as a major lipid-soluble chain-breaking antioxidant and a modulator of the immune system. A few well-designed studies with high levels of vitamin E supplementation in the elderly have shown a significant T-cell mediated immunostimulatory function with no adverse effects.^{7,8} Although the current RDA for vitamin E

is 8-10 mg/day, 20 percent of the population consumes less than half of the RDA. In general, an increased intake of 100-400 IU appears to provide protection against coronary heart disease and may decrease damage to DNA.⁹ However, in healthy well-nourished elderly subjects, vitamin E did not show a beneficial effect on respiratory infection¹⁰, whereas in elderly subjects with impaired immunity, supplementation with 100 mg was very beneficial indicating that the differences in vitamin E benefit may be related to the health of the elderly.¹¹ Furthermore, recent studies indicate that γ -tocopherol may be much more beneficial than α -tocopherol.¹² Thus, new studies are still required to focus on the type of vitamin E and the dose to define the benefits to the healthy elderly as well as in restoring immune function in immunocompromised elderly subjects.

Zinc: Zinc deficiency is known to cause immune dysfunction and increase the susceptibility to infection.¹³ At present, the adult requirement for zinc has been set at 12-15 mg, but 18 percent of the U.S. population may consume less than half of the RDA. Zinc deficiency not only causes deficiency of T-cell and B cell mediated immunity, but also increases in chromosome breakage from oxidative damage.^{14,15} Mild zinc deficiency decreases Th1 cytokines in the elderly and both impaired wound healing and diminished resistance to infection were improved by zinc supplementation¹⁶, but larger doses of zinc have been found to cause toxic effects on immune cells. Well-designed clinical dose-response studies in the elderly are needed to evaluate the relationship of plasma zinc to changes in Th-1 and Th-2 cytokines and to measure the restoration of innate and adaptive immune function, particularly in the elderly with chronic diseases of aging.

n-3 fatty acids: In recent years, an increased dietary n-6/n-3 fatty acid ratio has been linked to the increase in several inflammatory disorders including cardiovascular disease and several autoimmune diseases such as rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, lupus, etc.^{17,18} It is recommended that the present unhealthy 10-20/1 ratio of n-6 to n-3 fatty acids be reduced to 4/1 for general health and should be 2/1 during impaired health.¹⁹ Sources of n-3 fatty acids include green leafy vegetables, n-3 fatty acid enriched oils, fish, and generally n-3 (EPA and DHA) fatty acid (fish oil) supplements. A recent meta analysis of 11 trials showed reduced mortality due to myocardial infarction and sudden death in patients who were on n-3 fatty acid enriched diets.²⁰ The mechanism of protection include reduced pro-inflammatory cytokines, c-reactive protein, platelet activation and PGE-2 production as well as changes in signaling pathways, transcription factors, and gene expression.^{21, 22, 23} Other recognized benefits include reduced serum triglycerides, blood pressure, and protection against bone loss.²⁴ Overall, there are many beneficial effects of n-3 fatty acid supplements, yet several multi-center clinical trials to investigate the therapeutic value and the precise underlying molecular mechanism of action of various well-defined n-3 fatty acid products including enriched EPA and DHA fatty acids with and without anti-oxidant supplements should be conducted in healthy and elderly subjects with various chronic diseases.

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