

Health Benefits of Nutritional Supplements

Selected Abstracts

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Forward

The importance of nutrition for human health has long been recognized. Prior to 1960, interest in this field largely focused on the etiology and prevention of acute nutrient deficiency diseases such as scurvy, rickets, and pellagra. Some 50 essential nutrients (vitamins, minerals, antioxidants, cofactors, essential amino acids, essential fatty acids) were identified, and recommended daily intakes for those essential nutrients (e.g. Recommended Dietary Allowances or RDAs) were developed. These recommendations, in turn, proved to be valuable in eradicating acute nutrient deficiency diseases.

During the past 20-30 years, attention has shifted to the role of diet and nutrition in the pathogenesis of chronic degenerative diseases. Heart disease, some cancers, osteoporosis, type II diabetes, and macular degeneration are all known to have dietary risk factors, many of which involve chronic nutrient deficiencies. Importantly, these associations have been much more difficult to study, in large measure because of the time frames involved. Chronic degenerative diseases develop over decades (lifetimes), and it is extremely challenging to conduct research programs for such extended periods. Nevertheless, advances in epidemiological and clinical research have helped us learn a great deal about the impacts (positive and negative) of diet and essential nutrient intakes on long-term health.

During the past decade, the scientific and healthcare communities have paid increasing attention to the role of nutritional supplements (as components of diet) in preventing and treating chronic disease. Hundreds of scientific studies have been conducted and published. These studies span a broad range of health issues. They have employed a wide variety of methodologies. And they have produced both positive and negative results. In some areas (e.g. the role of calcium and vitamin D supplements in slowing the progression of osteoporosis, and the role of folic acid supplements in preventing certain birth defects), results have been consistent, and benefits have been well accepted. In other areas (e.g. the role of antioxidant supplementation in preventing heart disease), results have been less consistent, and conclusions remain controversial. In any event, research on the health benefits of nutritional supplements is progressing, and evidence continues to mount that nutritional supplements offer a convenient and cost effective means for promoting health, over both the short- and long-terms.

The following is a collection of abstracts from about 100 scientific papers describing research on the health benefits of nutritional supplements. This collection is not exhaustive. Papers were selected on the basis of scientific merit and relevance to the field. The majority describes positive results, but in some, negative results are reported. Our objective in compiling this list was to provide readers with a good cross section of the scientific literature so that they could develop a sense for the current state of research in this field and draw their own conclusions concerning the role of supplementation in healthcare. References for many more papers are given in our bibliography entitled *Health Benefits of Nutritional Supplements: Selected Readings* .

For convenience, the abstracts have been sorted by health issue; namely Cardiovascular Health, Cancer Prevention, Strong Bones, Healthy Pregnancies/Healthy Babies, Sound Metabolism, Robust Immune Function, Acute Vision, and Other.

Robust Immune Function

Effect of vitamin and trace-element supplementation on immune responses and infection in elderly subjects.

Chandra RK. 1992.
Lancet 340(8828):1124-7

Ageing is associated with impaired immune responses and increased infection-related morbidity. This study assessed the effect of physiological amounts of vitamins and trace elements on immunocompetence and occurrence of infection-related illness. 96 independently living, healthy elderly individuals were randomly assigned to receive nutrient supplementation or placebo. Nutrient status and immunological variables were assessed at baseline and at 12 months, and the frequency of illness due to infection was ascertained. Subjects in the supplement group had higher numbers of certain T-cell subsets and natural killer cells, enhanced proliferation response to mitogen, increased interleukin-2 production, and higher antibody response and natural killer cell activity. These subjects were less likely than those in the placebo group to have illness due to infections (mean [SD] 23 [5] vs 48 [7] days per year, $p = 0.002$). Supplementation with a modest physiological amount of micronutrients improves immunity and decreases the risk of infection in old age.

Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients: a randomized controlled trial. MIN. VIT. AOX. geriatric network.

Girodon F, Galan P, Monget AL, Boutron-Ruault MC, Brunet-Lecomte P, Preziosi P, Arnaud J, Manuguerra JC, Herchberg S. 1999.
Arch Intern Med 159(7):748-54

BACKGROUND: Antioxidant supplementation is thought to improve immunity and thereby reduce infectious morbidity. However, few large trials in elderly people have been conducted that include end points for clinical variables. **OBJECTIVE:** To determine the effects of long-term daily supplementation with trace elements (zinc sulfate and selenium sulfide) or vitamins (beta carotene, ascorbic acid, and vitamin E) on immunity and the incidence of infections in institutionalized elderly people. **METHODS:** This randomized, double-blind, placebo-controlled intervention study included 725 institutionalized elderly patients (>65 years) from 25 geriatric centers in France. Patients received an oral daily supplement of nutritional doses of trace elements (zinc and selenium sulfide) or vitamins (beta carotene, ascorbic acid, and vitamin E) or a placebo within a 2 x 2 factorial design for 2 years. **MAIN OUTCOME MEASURES:** Delayed-type hypersensitivity skin response, humoral response to influenza vaccine, and infectious morbidity and mortality. **RESULTS:** Correction of specific nutrient deficiencies was observed after 6 months of supplementation and was maintained for the first year, during which there was no effect of any treatment on delayed-type hypersensitivity skin response. Antibody titers after influenza vaccine were higher in groups that received trace elements alone or associated with vitamins, whereas the vitamin group had significantly lower antibody titers ($P < .05$). The number of patients without respiratory tract infections during the study was higher in groups that received trace elements ($P = .06$). Supplementation with neither trace elements nor vitamins significantly reduced the incidence of urogenital infections. Survival analysis for the 2 years did not show any differences between the 4 groups. **CONCLUSIONS:** Low-dose supplementation of zinc and selenium provides significant improvement in elderly patients by increasing the humoral response after vaccination and could have considerable public health importance by reducing morbidity from respiratory tract infections.

Effect of micronutrient supplementation on infection in institutionalized elderly subjects: a controlled trial.

Girodon F, Lombard M, Galan P, Brunet-Lecomte P, Monget AL, Arnaud J, Preziosi P, Hercberg S. 1997. *Ann Nutr Metab* 41(2):98-107

To determine the impact of a trace element and vitamin supplementation on infectious morbidity, a double-blind controlled trial was performed on 81 elderly subjects in a geriatric center during a 2-year period. Subjects were randomly assigned to one of four treatment groups, and received daily: placebo; trace elements/zinc 20 mg; selenium 100 micrograms); vitamins (vitamin C 120 mg; beta-carotene 6 mg; alpha-tocopherol 15 mg); or a combination of trace elements and vitamins at equal doses. (1) Before supplementation, low serum values in vitamin C, folate, zinc and selenium were observed in more than two thirds of the patients. (2) After 6 months of supplementation, a significant increase in vitamin and trace element serum levels was obtained in the corresponding treatment groups: a plateau was then observed for the whole study. (3) Subjects who received trace elements (zinc and selenium) alone or associated with vitamins had significantly less infectious events during the 2 years of supplementation. These results indicate that supplementation with low doses of vitamins and trace elements is able to rapidly correct corresponding deficiencies in the institutionalized elderly. Moreover, zinc and selenium reduced infectious events.

Vitamin E supplementation enhances cell-mediated immunity in healthy elderly subjects.

Meydani SN, Barklund MP, Liu S, Meydani M, Miller RA, Cannon JG, Morrow FD, Rocklin R, Blumberg JB. 1990. *Am J Clin Nutr* 52(3):557-63

The effect of vitamin E supplementation on the immune response of healthy older adults was studied in a double-blind, placebo-controlled trial. Subjects (n = 32) resided in a metabolic research unit and received placebo or vitamin E (800 mg dl-alpha-tocopheryl acetate) for 30 d. Alpha-tocopherol content of plasma and peripheral blood mononuclear cells (PBMCs), delayed-type hypersensitivity skin test (DTH), mitogen-stimulated lymphocyte proliferation, as well as interleukin (IL)-1, IL-2, prostaglandin (PG) E₂, and serum lipid peroxides were evaluated before and after treatment. In the vitamin E-supplemented group 1) alpha-tocopherol content was significantly higher (p less than 0.0001) in plasma and PBMCs, 2) cumulative diameter and number of positive antigen responses in DTH response were elevated (p less than 0.05), 3) IL-2 production and mitogenic response to optimal doses of concanavalin A were increased (p less than 0.05), and 4) PGE₂ synthesis by PBMCs (p less than 0.005) and plasma lipid peroxides (p less than 0.001) were reduced. Short-term vitamin E supplementation improves immune responsiveness in healthy elderly individuals; this effect appears to be mediated by a decrease in PGE₂ and/or other lipid-peroxidation products.

Short- and long-term beta-carotene supplementation do not influence T cell-mediated immunity in healthy elderly persons.

Santos MS, Leka LS, Ribaya-Mercado JD, Russell RM, Meydani M, Hennekens CH, Gaziano JM, Meydani SN. 1997.
Am J Clin Nutr 66(4):917-24

Supplementation of healthy elderly persons with beta-carotene has been considered a way to enhance immune responses. In study 1 the short-term effect of beta-carotene (90 mg/d for 3 wk) on immunity was assessed in a randomized, double-blind, placebo-controlled longitudinal comparison of healthy elderly women. In study 2 the long-term effect of beta-carotene (50 mg every other day for 10-12 y) on immunity was assessed in a randomized, double-blind, placebo-controlled longitudinal comparison of men enrolled in the Physicians' Health Study. Subjects from both studies taking active supplements had significantly greater plasma beta-carotene concentrations than did subjects taking placebo. The pre- to postintervention change in delayed-type hypersensitivity skin test responses between beta-carotene and placebo groups in the short-term study was not significantly different, nor was the response between treatment groups in the long-term study. There were no significant effects due to beta-carotene supplementation on in vitro lymphocyte proliferation, production of interleukin 2, or production of prostaglandin E2 as a result of short- or long-term beta-carotene supplementation. In addition, there were no differences in the profiles of lymphocyte subsets [total T cells (CD3+), T helper cells (CD4+), T cytotoxic-suppressor cells (CD8+), and B cells (CD19+)] due to short- or long-term beta-carotene supplementation, nor were there differences in percentages of CD16+ natural killer cells or activated lymphocytes (cells expressing interleukin 2 transferrin receptor) due to long-term beta-carotene supplementation. Consistent results from these two trials show that beta-carotene supplementation did not have an enhancing or suppressive effect on T cell-mediated immunity of healthy elderly.