

Beta carotene and Immunity

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Ingested beta-carotene enhances glutathione level and up-regulates the activity of cysteine cathepsin in murine splenocytes.

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To elucidate health benefits of beta-carotene, especially on immunity, we measured redox-related indices in spleen cells from BALB/c mice supplemented with various amounts of beta-carotene. In mice supplemented with beta-carotene in their diet, glutathione, an intracellular anti-oxidation agent, increased in their splenocytes. This change was highly correlated with the accumulation of beta-carotene, but not with that of retinol. The increase in glutathione was accompanied by an increase in mRNA for gamma-glutamylcysteine synthetase, a rate-limiting enzyme for glutathione synthesis. The higher the glutathione content was in the spleen cells, the higher the activity of cysteine cathepsin became in crude antigen-presenting cells contained in the spleen. These data suggest that accumulated beta-carotene in splenocytes, without being metabolized, caused an increase in the intracellular glutathione level, thereby anti-oxidatively supporting the activity of redox-sensitive lysosomal protease, which is involved in antigen-presentation.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 18540097 [PubMed - indexed for MEDLINE]

Maternal effects and beta-carotene assimilation in Canary chicks.

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Carotenoids are pigments responsible for the red, orange and yellow coloration of plants and animals. They may be beneficial in two ways; they have a powerful antioxidant activity, and they can behave as an immunostimulant. Animals however cannot synthesize carotenoids de novo, they must obtain them through their diet. In our experiments on Canaries, we investigated how mothers transfer their dietary carotenoid-related benefits to their offspring; either through the egg, or through the diet (during chicks' feeding). Female Canaries were allowed to access beta-carotene enriched food during egg formation and/or chicks' feeding. We sorted the chicks into four groups using the period when they assimilated the beta-carotene as a variable. The four groups were: (i) before hatching (from yolk), (ii) after hatching (from maternal feeding), (iii) before and after hatching, or (iv) never. Colorimetry and HPLC analysis from sub-samples of yolks confirmed the maternal transfer of dietary carotenoids to the yolk. Our results show that benefits from maternal dietary carotenoids are transferred to the chicks, but according to the period when they are assimilated by the chicks, the physiological effects are different. It was found that the chicks' growth was enhanced when carotenoids were assimilated both before and after hatching. However an increase in cellular immunity efficiency only occurs when the assimilation takes place after hatching.

Publication Types:

- [Comparative Study](#)

PMID: 19059274 [PubMed - indexed for MEDLINE]

Role of antioxidants and trace elements in health and immunity of transition dairy cows.

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A number of antioxidants and trace minerals have important roles in immune function and may affect health in transition dairy cows. Vitamin E and beta-carotene are important cellular antioxidants. Selenium (Se) is involved in the antioxidant system via its role in the enzyme glutathione peroxidase. Inadequate dietary vitamin E or Se decreases neutrophil function during the perparturient period. Supplementation of vitamin E and/or Se has reduced the incidence of mastitis and retained placenta, and reduced duration of clinical symptoms of mastitis in some experiments. Research has indicated that beta-carotene supplementation may enhance immunity and reduce the incidence of retained placenta and metritis in dairy cows. Marginal copper deficiency resulted in reduced neutrophil killing and decreased interferon production by mononuclear cells. Copper supplementation of a diet marginal in copper reduced the peak clinical response during experimental *Escherichia coli* mastitis. Limited research indicated that chromium supplementation during the transition period may increase immunity and reduce the incidence of retained placenta.

Publication Types:

- [Review](#)

PMID: 18325801 [PubMed - indexed for MEDLINE]

Yolk testosterone levels and dietary carotenoids influence growth and immunity of grey partridge chicks.

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Early maternal effects in the form of substances accumulated in the egg, such as carotenoids and hormones, can be physiologically relevant for a good development of offspring. It has been found in different species that testosterone (T) can be beneficial to offspring by increasing growth rate, but detrimental by reducing immunocompetence and increasing oxidative stress. Carotenoids on the other hand are suggested to be beneficial because they can counteract the oxidative stress and the immune-depressive effect of T. In this study we analyzed the effect of prenatal T exposure in the grey partridge. We injected eggs with three doses of T (high, intermediate, and physiological). After hatching, chicks exposed to a prenatal high dose of T were fed with two diets (rich or poor) differing in beta-carotene content. We found a significant effect of T on both chick growth and cell-mediated immunity, with high T doses resulting in detrimental effects while low doses were beneficial. Detrimental effects of the high dose of T on immunity were mitigated by beta-carotene consumed in the diet. The differences between groups were observed in the early period of life (age 10 days for mass, and age 10 and 21 days for immunity), and disappeared in the following period, and up to 1 and 2 years later. Overall, our observations show that T in the egg is not detrimental but beneficial, and that negative effects are found only at supraphysiological concentrations. The negative effects of T on immunity could be balanced if chicks could consume a diet rich in beta-carotene.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

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Effects of beta-carotene on adult immune condition and antibacterial activity in the eggs of the Grey Partridge, *Perdix perdix*.

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Carotenoids are important dietary constituents in birds. Their functions are numerous and complex, and breeding females are potentially faced with an optimal allocation of these resources between themselves and offspring. We conducted a dietary experiment (low and high supply of beta-carotene) to examine the effect of beta-carotene on health and immune response of 64 reproducing pairs of Grey Partridge (*Perdix perdix* L.) and on the quality of their eggs, as revealed by the measurement of biochemical components in yolk and albumen, the egg hatching rate and chick survival. We found a beneficial effect of beta-carotene on the erythro sedimentation rate and immune response of females (PHA reaction), while the diet did not significantly affect these variables in males. In both sexes, the plasma level of carotenoids was not related to the quantity of beta-carotene supplied. A higher quantity of beta-carotene in the diet did not induce a variation of egg nutrients (proteins and lipids), nor an increase of yolk beta-carotene concentration. We detected a higher concentration of lysozyme, an enzyme with antibacterial activity, in the albumen of eggs laid by females with a high supply of beta-carotene. These eggs showed higher hatching rates. The present study indicates that although carotenoid supplementation does not influence blood and yolk carotenoid levels, it results in better immune conditions of females, eventually translated into increased antibacterial activity of the eggs. The broad range of beneficial effects of carotenoids is discussed.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 17462926 [PubMed - indexed for MEDLINE]

Immunity and antioxidant capacity in humans is enhanced by consumption of a dried, encapsulated fruit and vegetable juice concentrate.

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The daily consumption of fruits and vegetables is a common dietary recommendation to support good health. We hypothesized that a commercially available encapsulated fruit and vegetable juice powder concentrate (FVJC) could support functional indices of health due to increased intake of various phytonutrients. This was a double-blind, randomized, placebo-controlled investigation of 59 healthy law students who consumed either FVJC or placebo capsules for 77 d. Blood was collected on d 1, 35, and 77 to examine the number of circulating alphabeta- and gammadelta-T cells, cytokine production, lymphocyte DNA damage, antioxidant status, and levels of carotenoids and vitamin C. A log of illnesses and symptoms was also kept. The FVJC group tended to have fewer total symptoms than the placebo group ($P < 0.076$). By d 77 there was a 30% increase in circulating gammadelta-T cells and a 40% reduction in DNA damage in lymphocytes in the FVJC group relative to the placebo group. Plasma levels of vitamin C and of beta-carotene, lycopene, and lutein increased significantly from baseline in the FVJC group as did plasma oxygen radical absorptive capacity (50%). Interferon-gamma produced by phorbol-stimulated lymphocytes was reduced 70% in the FVJC group, whereas other cytokines (IL-4, IL-6, transforming growth factor beta) were unchanged relative to treatment or time. FVJC consumption during this study period resulted in increased plasma nutrients and antioxidant capacity, reduction in DNA strand breaks, and an increase in circulating gammadelta-T cells.

Publication Types:

- [Randomized Controlled Trial](#)
- [Research Support, Non-U.S. Gov't](#)

PMID: 16988134 [PubMed - indexed for MEDLINE]

Effects of beta-carotene supplementation on chick growth, immune status and behaviour in the grey partridge, *Perdix perdix*.

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Carotenoids are important for various functions during chick development. Since these pigments cannot be synthesized, they can be considered limited resources that the mother optimally allocates between herself and her offspring (maternal effect). Some studies have examined the effects of carotenoids on growth and immune function but little is known about their role in behaviour. In this study of the grey partridge, we conducted two supplementation experiments: (1) laying females were fed with beta-carotene enriched or impoverished diets; (2) chicks were fed directly with beta-carotene enriched or impoverished diets. We then evaluated the effects of this carotenoid on chick growth, immunocompetence and anti-predator behaviour (reactions to a raptor model). In the first experiment, the beta-carotene enriched diet given to mothers did not cause any difference in chick physiology. In the second experiment, beta-carotene supplementation of chicks had a significant beneficial effect on their growth and immune response, although their behavioural reactions did not differ in relation to the diet. Therefore, beta-carotene supplementation had beneficial effects on growth and immunocompetence only when directly supplied to chicks. The beneficial effect reported in other species for begging or pecking behaviours was not confirmed for the anti-predator behaviour of grey partridge chicks.

Publication Types:

- [Comparative Study](#)
- [Research Support, Non-U.S. Gov't](#)

PMID: 16963199 [PubMed - indexed for MEDLINE]

[Clin Exp Allergy](#). 2006 Aug;36(8):993-1000.

Associations between antioxidant status, markers of oxidative stress and immune responses in allergic adults.

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BACKGROUND: There has been growing interest in the role of antioxidant function in controlling inflammatory disease states, such as allergy. This study investigated the relationship between antioxidant status, markers of airways inflammation [exhaled nitric oxide (eNO)], oxidative stress (F(2) isoprostanes) and immune responses in allergic adults. **METHODS:** Antioxidants (vitamins C, E, beta-carotene and selenium) and total antioxidant capacity (tAC) in serum were examined in relation to eNO, plasma F(2) isoprostanes and peripheral blood mononuclear cell (PBMC) cytokine and lymphoproliferative response to house dust mite (HDM) allergen, Staphylococcus enterotoxin B (SEB), phytohaemagglutinin (PHA) and lipopolysaccharide (LPS) in 54 allergic adults. **RESULTS:** Firstly, levels of specific vitamins did not correlate with tAC. Secondly, we did not see any evidence that specific vitamin levels (or tAC) were associated with either polarization or attenuation of in vitro immune responses. If anything, there were positive correlations between antioxidant (vitamin C and selenium) levels and HDM allergen responses [lymphoproliferation (selenium; $r=0.35$, $P=0.013$) and both Th2 IL13 (vitamin C; $\tau=0.254$, $P=0.028$) and Th1 IFN-gamma (vitamin C; $\tau=0.302$, $P=0.009$) responses]. There were also significant positive relationships between antioxidant levels and IL-10 responses to polyclonal stimulation by SEB ($r=0.292$, $P=0.036$) and LPS ($r=0.34$, $P=0.015$) (beta-carotene) and PHA ($r=0.34$, $P=0.021$) (tAC). Thirdly, although airways inflammation (eNO) was associated with both in vitro and in vivo (skin test reactivity) to HDM, we did not see any correlation between eNO and oxidative stress (F(2)-isoprostanes). Finally, there were no consistent relationships between oxidative stress and immune responses. **CONCLUSION:** There was no evidence that higher antioxidant levels were associated with reduced allergen responsiveness in allergic adults. If anything, antioxidant status was associated with increased immune responsiveness. The significance of this needs to be addressed in future intervention studies.

Publication Types: [Research Support, Non-U.S. Gov't](#)

Natural beta-carotene for the prevention of post-ERCP pancreatitis.

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OBJECTIVE: Endoscopic retrograde cholangiopancreatography (ERCP) is a commonly used procedure. Pancreatitis is its most common complication. As the injury may be mediated by oxidative stress, it could be ameliorated by antioxidants. **METHODS:** We conducted a double-blind trial, giving the patients a single dose of natural beta-carotene or placebo, 12 hours prior to procedure, and monitoring them for 24 hours post-procedure for procedure complications, antioxidant levels, and plasma oxidation. **RESULTS:** The overall incidence of acute pancreatitis according to our definition was 9.6%. The incidence of pancreatitis was not significantly different between the beta-carotene group (10%) and the placebo group (9.4%). Four patients in the placebo group had severe pancreatitis (2.22%), but none in the beta-carotene group. This difference is statistically significant. **CONCLUSION:** We did not see a reduction in the incidence of post-ERCP pancreatitis, but there may be some protective effect of treatment with beta-carotene regarding the severity of disease.

Publication Types:

- [Clinical Trial](#)
- [Comparative Study](#)
- [Randomized Controlled Trial](#)

PMID: 15257114 [PubMed - indexed for MEDLINE]

Enhancement of innate immunity in rainbow trout (*Oncorhynchus mykiss* Walbaum) associated with dietary intake of carotenoids from natural products.

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The effects of orally administered carotenoids from natural sources on the non-specific defense mechanisms of rainbow trout were evaluated in a nine-week feeding trial. Fish were fed four diets containing either beta-carotene or astaxanthin at 100 and 200 mg kg⁻¹ from the marine algae *Dunaliella salina* and red yeast *Phaffia rhodozyma*, respectively, and a control diet containing no supplemented carotenoids. Specific growth rate and feed:gain ratio were not affected by dietary carotenoid supplementation. Among the humoral factors, serum alternative complement activity increased significantly in all carotenoid supplemented groups when compared to the control. On the other hand, serum lysozyme activity increased in the *Dunaliella* group but not in the *Phaffia* group, whereas plasma total immunoglobulin levels were not altered by the feeding treatments. As for the cellular responses, the superoxide anion production from the head kidney remained unchanged while the phagocytic rate and index in all supplemented groups were significantly higher than those of the control. These findings demonstrate that dietary carotenoids from both *D. salina* and *P. rhodozyma* can modulate some of the innate defense mechanisms in rainbow trout.

Publication Types:

- [Comparative Study](#)
- [Research Support, Non-U.S. Gov't](#)

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[J Nutr.](#) 2004 Jan;134(1):257S-261S.

Carotenoid action on the immune response.

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Early studies demonstrating the ability of dietary carotenes to prevent infections have left open the possibility that the action of these carotenoids may be through their prior conversion to vitamin A. Subsequent studies to demonstrate the specific action of dietary carotenoids have used carotenoids without provitamin A activity such as lutein, canthaxanthin, lycopene and astaxanthin. In fact, these nonprovitamin A carotenoids were as active, and at times more active, than beta-carotene in enhancing cell-mediated and humoral immune response in animals and humans. Another approach to study the possible specific role of dietary carotenoids has used animals that are inefficient converters of carotenoids to vitamin A, for example the domestic cat. Results have similarly shown immunoenhancement by nonprovitamin A carotenoids, based either on the relative activity or on the type of immune response affected compared to beta-carotene. Certain carotenoids, acting as antioxidants, can potentially reduce the toxic effects of reactive oxygen species (ROS). These ROS, and therefore carotenoids, have been implicated in the etiology of diseases such as cancer, cardiovascular and neurodegenerative diseases and aging. Recent studies on the role of carotenoids in gene regulation, apoptosis and angiogenesis have advanced our knowledge on the possible mechanism by which carotenoids regulate immune function and cancer.

Publication Types:

- [Review](#)

PMID: 14704330 [PubMed - indexed for MEDLINE]

Effects of age and dietary beta-carotene on immunological variables in dogs.

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beta-Carotene is a naturally occurring carotenoid reported to have health-promoting effects in several species. Advancing age is known to have a negative impact on various immune variables in several species. This study was conducted in order to assess the effect of age on immune response in dogs and to determine whether beta-carotene is able to reverse this age-associated decline. To test this hypothesis, young and old dogs (n = 36) were fed either a control diet or experimental diets containing supplemental beta-carotene for 2-month periods. Age significantly (P < .05) lowered CD4+ T cell populations (47.2% versus 33.7%; young-control versus old-control, respectively) and beta-carotene restored percent distributions in old dogs to nonsignificance versus younger controls (41.0%). T cell proliferation was lower in old dogs (30,254 +/- 2,248 versus 14,811 +/- 2,497 cCPM; young-control versus old-control, respectively; P < .05), and beta-carotene supplementation significantly improved responses in this age group (21,329 +/- 2,275 cCPM). Although B cell proliferation was depressed with age (17,967 +/- 1,384 versus 7,535 +/- 1,469 cCPM; young-control versus old-control, respectively; P < .05), beta-carotene supplementation improved B cell proliferation in young dogs (23,500 +/- 1,339 cCPM). Old dogs displayed lower delayed-type hypersensitivity test (DTH) responses versus younger controls to both phytohemagglutinin-P (PHA; 11.1 +/- 0.95 versus 7.57 +/- 1.15 mm; young-control versus old-control, respectively; P < .05) and sheep red blood cell (RBC; 9.12 +/- 0.62 versus 8.08 +/- 0.75 mm; young-control versus old-control, respectively; P < .10). beta-Carotene improved these responses, mostly within the first 24-48 hours after injection. In summary, older dogs have lower immunological responses compared with younger controls. beta-Carotene supplementation significantly restored immune responses in older dogs when compared with their age-matched controls and younger counterparts.

PMID: 14658721 [PubMed - indexed for MEDLINE]

Micronutrients and innate immunity.

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Micronutrients such as zinc, selenium, iron, copper, beta-carotene, vitamins A, C, and E, and folic acid can influence several components of innate immunity. Select micronutrients play an important role in alteration of oxidant-mediated tissue injury, and phagocytic cells produce reactive oxidants as part of the defense against infectious agents. Thus, adequate micronutrients are required to prevent damage of cells participating in innate immunity. Deficiencies in zinc and vitamins A and D may reduce natural killer cell function, whereas supplemental zinc or vitamin C may enhance their activity. The specific effects of micronutrients on neutrophil functions are not clear. Select micronutrients may play a role in innate immunity associated with some disease processes. Future studies should focus on issues such as age-related micronutrient status and innate immunity, alterations of micronutrients in disease states and their effect on innate immunity, and the mechanisms by which micronutrients alter innate immunity.

Publication Types:

- [Review](#)

PMID: 10944478 [PubMed - indexed for MEDLINE]

[J Nutr.](#) 2000 Aug;130(8):1910-3.

Dietary beta-carotene stimulates cell-mediated and humoral immune response in dogs.

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The role of beta-carotene on immune response in domestic dogs is not known. Female Beagle dogs were fed 0, 2, 20 or 50 mg beta-carotene/d; blood was sampled at wk 0, 1, 2, 4 and 8 for analysis of the following: lymphoproliferation, leukocyte subpopulations and concentrations of interleukin-2 (IL-2), immunoglobulin (Ig)G and IgM. Delayed-type hypersensitivity (DTH) response was assessed at wk 0, 3 and 7. beta-Carotene supplementation increased plasma beta-carotene concentrations in a dose-dependent manner. Compared with unsupplemented dogs, those fed 20 or 50 mg of beta-carotene had higher CD4+ cell numbers and CD4:CD8 ratio. However, there was no treatment difference in CD8+, CD21+ and major histocompatibility complex (MHC) class II+ cells. Plasma IgG, but not IgM concentration was higher in dogs fed beta-carotene throughout the study period. The DTH response to phytohemagglutinin (PHA) and vaccine was heightened in beta-carotene-supplemented dogs. beta-Carotene feeding did not influence mitogen-induced lymphocyte proliferation or IL-2 production. Immune response was impaired in dogs classified as low beta-carotene absorbers compared with similar dogs fed the same amount of beta-carotene. Therefore, dietary beta-carotene heightened cell-mediated and humoral immune responses in dogs.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 10917901 [PubMed - indexed for MEDLINE]

[Clin Infect Dis.](#) 1998 Mar;26(3):711-8.

The significance of vitamin A and carotenoid status in persons infected by the human immunodeficiency virus.

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Hyporetinemia is associated with increased childhood morbidity and mortality that is reversible with vitamin A supplementation. Although vitamin A deficiency is otherwise rare in developed countries, the prevalence of hyporetinemia in human immunodeficiency virus (HIV)-infected persons is up to 29%. Hyporetinemic HIV-infected patients have a 3.5-5-fold increased risk of death. Furthermore, HIV-infected patients with very low or very high intake of vitamin A and beta-carotene (a vitamin A precursor) have greater rates of disease progression than do patients with intermediate intake. In developing countries up to 60% of HIV-infected pregnant women are hyporetinemic. In such women the relative risk of perinatal HIV transmission may be increased more than fourfold. These data indicate that vitamin A deficiency is common in HIV-infected patients in the developed world and strongly suggest that vitamin A supplementation may be especially useful in adjunctive therapy for HIV-infected pregnant women who reside in the developing world.

Publication Types:

- [Review](#)

PMID: 9524850 [PubMed - indexed for MEDLINE]