NEOLIFE

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NEOLIFE STUDIES

Modulated mitogenic proliferative responsiveness of lymphocytes in whole-blood cultures after a low-carotene diet and mixed-carotenoid supplementation in women

ABSTRACT
To determine the effects of dietary carotenes on the mitogenic proliferative responsiveness of blood lymphocytes in vitro, nine premenopausal women were fed a low-carotene diet for 120 d. Low-dose beta-carotene (0.5 mg/d) was given to five subjects on days 1-60, while four received a placebo. All subjects received a low-dose beta-carotene (0.5 mg/d) supplement on days 61-120, plus a carotenoid complex on days 101-120. The mean (+/-SEM) serum beta-carotene concentration for the combined beta-carotene supplemented and placebo subjects (n = 9) was not significantly reduced from that on day 1 (1.27 +/- 0.24 mumol/L) on days 60 (0.66 +/- 0.14 mumol/L) and 100 (0.91 +/- 0.38 mumol/L), but on day 120 (3.39 +/- 0.44 mumol/L) it was increased above that on days 1, 60, and 100. Maximum mitogenicproliferative responsiveness of blood lymphocytes in vitro to optimal dose phytohemagglutinin (PHA) was reduced on days 60 (P = 0.025) and 100 (P < 0.0001), but corrected itself on day 120 to a value above those on day 1 (P = 0.04), day 60 (P = 0.0001), and day 100 (P < 0.0001). Present findings show that a diet low in carotene had a suppressive effect on the maximum mitogenic proliferative responsiveness of bloodlymphocytes in vitro, which was not corrected with low-dose beta-carotene supplementation but was with a carotenoid complex from vegetables rich in carotenoids.

Source
http://carotenoidcomplex.com/pdfs/Modulated.pdf

Plasma carotenoid concentrations before and after supplementation with a carotenoid mixture

ABSTRACT
Plasma carotenoid concentrations were determined by HPLC in 11 individuals consuming low-carotenoid diets and after taking a carotenoidsupplement. Subjects first consumed low-carotenoid diets for 2 wk, then supplemented these diets daily with 8.5 mg beta-carotene, 3.5 mg alpha-carotene, and 0.5 mg lycopene, from natural sources for 4 wk. Serum cholesterol, triglycerides, and lipoproteins were determined before and after supplementation. After 2 wk on the low-carotenoid diet, plasma concentrations of the three carotenoids fell to approximately 60% of baseline values. One week after supplementation, alpha- and beta-carotene concentrations returned to baseline and by the end of thesupplementation period they were significantly higher than baseline values (P < 0.05). Lycopene concentrations increased only slightly. Serum lipids did not change significantly. Overall, plasma concentrations of these carotenoids reflect the amount provided by the supplement. This is the first study reporting increments of serum carotenoids, other than beta-carotene, after supplementation.

Source
http://carotenoidcomplex.com/pdfs/Plasma.pdf

5-Lipoxygenase Metabolite 4-HDHA Is a Mediator of the Antiangiogenic Effect of ω-3 Polyunsaturated Fatty Acids

ANTI-ANGIOGENESIS
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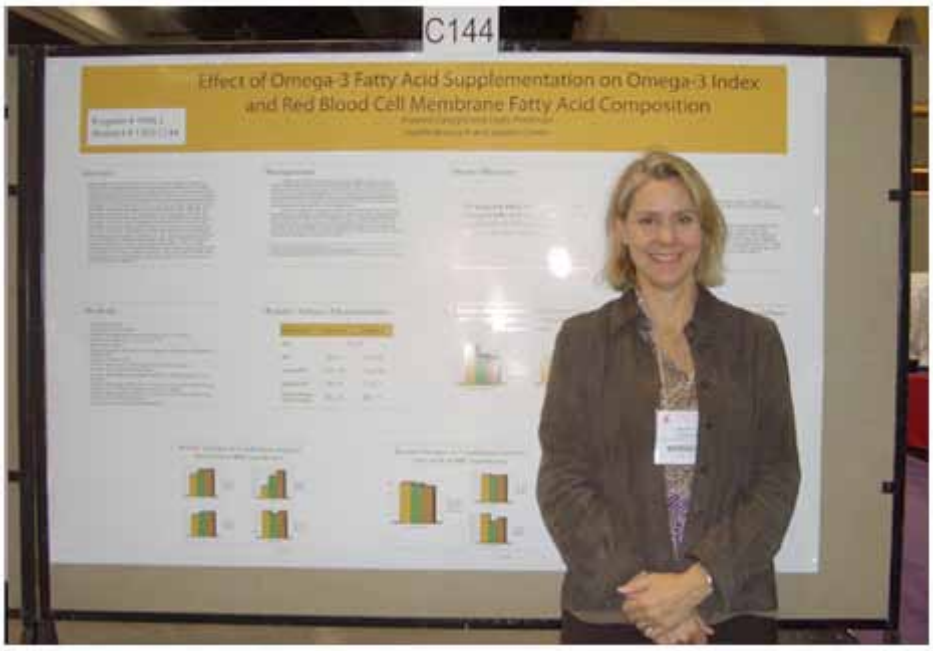
ABSTRACT
Lipid signaling is dysregulated in many diseases with vascular pathology, including cancer, diabetic retinopathy, retinopathy of prematurity, and age-related macular degeneration. We have previously demonstrated that diets enriched in ω-3 polyunsaturated fatty acids (PUFAs) effectively reduce pathological retinal neovascularization in a mouse model of oxygen-induced retinopathy, in part through metabolic products that suppress microglial- derived tumor necrosis factor–a. To better understand the protective effects of ω-3 PUFAs, we examined the relative importance of major lipid metabolic pathways and their products in contributing to this effect. ω-3 PUFA diets were fed to four lines of mice deficient in each key lipid-processing enzyme (cyclooxygenase 1 or 2, or lipoxygenase 5 or 12/15), retinopathy was induced by oxygen exposure; only loss of 5-lipoxygenase (5-LOX) abrogated the protection against retinopathy of dietary ω-3 PUFAs. This protective effect was due to 5-LOX oxida-tion of the ω-3 PUFA lipid docosahexaenoic acid to 4-hydroxy-docosahexaenoic acid (4-HDHA). 4-HDHA directly inhibited endothelial cell proliferation and sprouting angiogenesis via peroxisome proliferator–activated receptor γ (PPARγ), independent of 4-HDHA's anti-inflammatory effects. Our study suggests that ω-3 PUFAs may be profit-ably used as an alternative or supplement to current anti–vascular endothelial growth factor (VEGF) treatment for proliferative retinopathy and points to the therapeutic potential of ω-3 PUFAs and metabolites in other diseases of vasoproliferation. It also suggests that cyclooxygenase inhibitors such as aspirin and ibuprofen (but not lipoxygenase inhibitors such as zileuton) might be used without losing the beneficial effect of dietary ω-3 PUFA.

Source
Science Translational Medicine, Vol. 3, Issue 69, Pages 1-12: "5-Lipoxygenase Metabolite 4-HDHA Is a Mediator of the Antiangiogenic Effect of w-3 Polyunsaturated Fatty Acids." February 09, 2011

Effect of Omega-3 Fatty Acid Supplementation on Omega-3 Index and Red Blood Cell (RBC) Membrane Fatty Acid Composition

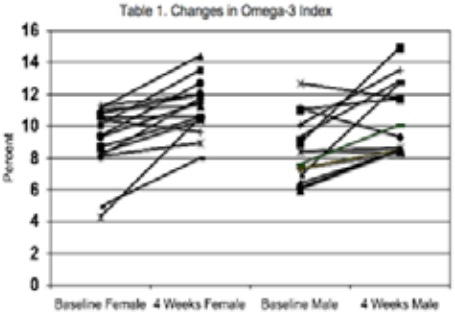
FASEB



Omega III Salmon Oil Plus Published in FASEB online Journal April 2008

ABSTRACT

Omega-3 fatty acids (n-3 FA) have been shown from epidemiological studies and clinical trials to reduce the incidence of cardiovascular disease (CVD) in patients with the pre-existing CVD as well as in healthy individuals. In randomized secondary prevention trials fish or fish oil have been shown to reduce total and coronary heart disease (CHD) mortality at intakes of about 1 g/day. The Omega-3 Index (EPA + DHA expressed as % of total fatty acid) has been proposed as a physiologically relevant, modifiable, independent and graded risk factor for death from CHD. RBC membrane fatty acid composition correlates well with biomarkers of n-3 FA including serum EPA and DHA, whole blood EPA, DPA and DHA and fatty acid composition of cardiac tissue. The present dietary intervention study investigates the effect of a fish-oil based, n-3 FA supplement on Omega-3 Index and RBC fatty acid composition. Thirty healthy men and women consumed a supplement providing 1070 mg total n-3 FA (460 mg DHA, 480 mg EPA, and 80 mg other n-3 FA) daily for 4 wks. At the end of this period there was a significant 23% increase ($p<0.01$) in the Omega-3 Index (Fig.1). While there were no significant changes in % linoleic, gamma linoleic, and alpha linolenic acid; EPA, DPA and DHA significantly ($p<0.01$) increased compared to baseline values (0.76% versus 1.4%; 2.30% versus 2.58% and 5.49% versus 6.60% respectively. There was a decrease ($p<0.05$) in arachidonic acid 19.58% versus 18.83%). This study shows that RBC membrane fatty acid composition and so Omega-3 Index can change in a short period of time with a fish-oil based supplement.



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Harris, WS, von Schacky C: The Omega-3 Index: A new risk factor for sudden cardiac death? Prev. Med. 2004, 39:212-220.

Harris et al. Omega-3 Fatty Acids in Cardiac Biopsies from Heart Transplant Patients: Correlation with Erythrocytes and Response to Supplementation. Circulation. 2004

http://www.gnldcontent.com/omega3/us/faseb.html

Reduced Cardiovascular Risk by Lowering Inflammatory Index

AMERICAN INCORPORATED A.C.N. COLLEGE OF NUTRITION

ABSTRACT

Carughi A. and Perelman D. Health Research & Studies Center, Los Altos, CA. Epidemiological and clinical studies have shown the cardio-protective effects of omega-3 (n-3) FA in patients with pre-existing cardiovascular disease and in healthy individuals. While mechanisms of action are not fully understood, n-3 FA are known to influence eicosanoid generating systems from membrane phospholipids and to lower proinflammatory circulating lipids. This study investigated the effects of low dose, marine sourced n-3 FA supplementation on selected markers of cardiovascular health and inflammation in

healthy, normo-triglyceridemic volunteers. Thirty-one men and women took a supplement providing 1070 mg n-3 FA, comprising 480 mg docosahexaenoic acid (DHA), 460 mg eicosapentaenoic acid (EPA), 50 mg docosapentaenoic acid (DPA) and 80 mg other n-3 FA daily for 8 wks. At the end of the supplementation period, % EPA, DHA and DPA in red blood cell membranes (RBCm) were higher than baseline values ($p<0.01$). Although neither % linoleic acid nor γ linolenic acid in RBCm change, % arachidonic acid (AA) was significantly lower. There was a 38% increase ($p<0.01$) in the omega-3 index (%DHA + %EPA in RBCm; 6.1 ± 1.8 vs. 8.5 ± 1.8) and a 17% reduction ($p<0.01$) in serum triglycerides. Lp-PLA2 levels were slightly higher after supplementation (147 ± 43 vs. 157 ± 51 nm/mL) but were within the normal range. While IL-6 levels did not change, inflammatory index was significantly lower (%AA:%EPA in RBCm; 2.5 ± 1.8 vs. 0.8 ± 1.2). This study shows that low dose, marine sourced n-3 supplementation for just 8 weeks can have a positive effect on markers of cardiovascular health and inflammation.

Source
http://www.gnldcontent.com/omega3/us/ACN.html

Effect of Omega-3 Fatty Acid Supplementation on Cardiovascular Risk Factors and Inflammatory Markers

Linus Pauling Institute

ABSTRACT
Diets rich in omega-3 fatty acids (n-3 FA) are associated with lower cardiovascular (CV) morbidity and mortality. Numerous mechanisms, including triglyceride-lowering and anti-inflammatory effects, have been proposed to explain the protective action of n-3 FA. We investigated the effect of marine-sourced n-3 FA supplementation on CVD risk factors and on markers of inflammation in healthy, normotriglyceridemic volunteers. Thirty-one men and women took a supplement providing 1070 mg total n-3 FA (480 mg docosahexaenoic acid, DHA; 460 mg eicosapentaenoic acid, EPA; 50 mg docosapentaenoic acid, DPA; and 80 mg other n-3 FA) daily for 8 wks. By 4 wks, values for % EPA, DPA, and DHA in red blood cell (RBC) membranes were significantly higher than at baseline, and kept increasing until the end of the study, when they were 56%, 16%, and 19% higher ($p < 0.01$, 0.05, and 0.01, respectively). While there were no changes in % linoleic acid or % -linolenic acid in RBC membranes, % arachidonic acid was 10% lower after supplementation ($p < 0.05$). At 8 wks serum triglyceride levels were 17% lower ($p < 0.01$), Omega-3 Index (% DHA + EPA in RBC) was 38% higher ($p < 0.01$), and the omega-6/omega-3 ratio was 30% lower ($p < 0.05$) than at baseline. Lp-PLA2 levels were slightly higher (147 ± 43 and 157 ± 51; $p<0.05$) but well within the normal range. While there were no significant changes in IL-6 and TNFa levels, Inflammatory Index was 68% lower (%AA: %EPA in RBC; $p<0.01$) after supplementation. This study shows that supplementation with relatively low levels of marine-sourced omega-3 fatty acids can quickly improve cardiovascular risk factors and modify fatty acid RBC membrane composition consistent with a lower inflammatory state.

Source
http://www.gnldcontent.com/omega3/us/Linus.html

Impact of Dietary Omega-3 and Omega-6 PUFA on DHA-derived Protective Autacoid Circuits

Gronert, Karsten and Leedom, Alexander from University of California, Berkeley, Vision Science Program, School of Optometry, Berkeley, CA

Carughi, Arianna and Perelman, Dalia from Health Research and Studies Center, Los Altos, CA

The Western diet contains 20-25 fold more omega-6 than omega-3 PUFA. Based on population studies and clinical trials omega-3 PUFA have been specifically recommended for the prevention of cardiovascular disease, and disorders with an inflammatory component such as retinopathies, rheumatoid arthritis and asthma. However, the mechanism for the beneficial effect of omega-3 PUFA is just beginning to unfold. DHA is a significant omega-3 PUFA in all human tissues and, more importantly, its levels are directly dependent on diet. The discovery of antiinflammatory DHA-derived mediators, protectin D1 (PD1) and 17S-resolvins, provides new insights into mechanisms for the anti-inflammatory effect of dietary omega-3 PUFA. We assessed the impact of short-term dietary omega-3 PUFA and omega-6 PUFA supplementation on lipid mediator profiles and outcome of acute and chronic inflammation in mice. Short-term dietary manipulation of omega-3/omega-6 PUFA dramatically altered formation of eicosanoids and DHA-derived mediators and extend of inflammatory injury and pathological neovascularization. Protective DHAderived mediators, 17-HDHA and PD1,

were formed at significantly levels in mice, human corneas and serum from healthy human volunteers. More importantly, an 8-week clinical trial with 30 healthy volunteers demonstrated that fish oil supplements caused only a small significant change in tissue DHA, EPA and AA levels. However, lipidomic analyses of clotted blood from these volunteers demonstrated a striking and selective inhibition of leukocyte lipoxygenase activity. Our findings demonstrate that subtle changes in omega-3 PUFA tissue levels are sufficient to markedly alter the state of leukocyte activation and add to a rapidly evolving paradigm, namely that formation of DHA-derived signals constitutes a resident anti-inflammatory circuit that is amenable to dietary amplification.
Supported in part by grants from the National Eye Institute (EY016136 and P30EY003176)

Source
http://www.gnldcontent.com/omega3/US/Gronert.html

PEER REVIEWED STUDIES

ABSORPTION OF CAROTENOIDS

Influence of olive oil on carotenoids bioavailability—A review

ABSTRACT
Bioavailability is defined as "the fraction of an ingested nutrient that is available for utilization in normal physiological functions or for storage". Available studies on carotenoids bioavailability are based on the measurement of their levels in serum or plasma. Dietary components were reported to affect the rate of carotenoids absorption. On digestion, carotenoids are incorporated into the lipid phase and then are emulsified into small lipid droplets. The nature and amount of lipids in the diet greatly affect the emulsification, secretion of bile salts, and formation of mixed micelles all of which are currently important subjects to understand the carotenoids bioavailability. Specific lipids, vegetable oils and their fatty acid moiety have been shown to affect the mixed micelles formation that positively influences the absorption of carotenoids. Gavages and dietary studies revealed that oleic acid micelles and olive oil (oleic acid, C18:1) enhance the intestinal accessibility of carotenoids more than linoleic acid micelles or vegetables oils rich in polyunsaturated fatty acids (PUFA). The chemistry of fats or oils which may act differently at various stages of absorption and metabolism of carotenoids is discussed. This review shows that dietary unsaturated fat appears to be a suitable carrier for carotenoids when oxidative stress is a critical issue in nutrition-related degenerative disorders.

Source
Lakshminarayana R et al. Influence of olive oil on carotenoids bioavailability—A review. Eur J Lipid Sci Tech DOI: 10.1002/ejlt.201200254, Epub ahead of print, 2012.

BLOOD SUGAR BALANCE

Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis

ABSTRACT
OBJECTIVE:
To investigate the independent effects of intake of fruit and vegetables on incidence of type 2 diabetes.

DESIGN:
Systematic review and meta-analysis.

DATA SOURCES:
Medline, Embase, CINAHL, British Nursing Index (BNI), and the Cochrane library were searched for medical subject headings and keywords on diabetes, prediabetes, fruit, and vegetables. Expert opinions were sought and reference lists of relevant articles checked.

STUDY SELECTION:
Prospective cohort studies with an independent measure of intake of fruit, vegetables, or fruit and vegetables and data on incidence of type 2 diabetes.

RESULTS:
Six studies met the inclusion criteria; four of these studies also provided separate information on the consumption of green leafy vegetables. Summary estimates showed that greater intake of green leafy vegetables was associated with a 14% (hazard ratio 0.86, 95% confidence interval 0.77 to 0.97) reduction in risk of type 2 diabetes (P=0.01). The summary estimates showed no significant benefits of increasing the consumption of vegetables, fruit, or fruit and vegetables combined.

CONCLUSION:
Increasing daily intake of green leafy vegetables could significantly reduce the risk of type 2 diabetes and should be investigated further.

Source
Carter P, et al. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. BMJ. 2010 Aug 18;341:c4229. doi: 10.1136/bmj.c4229.

Magnesium intake and risk of type 2 diabetes: a meta-analysis

ABSTRACT
OBJECTIVE:
To assess the association between magnesium intake and risk of type 2 diabetes.

DESIGN:
Meta-analysis of prospective cohort studies.

DATA SOURCES:
We retrieved studies published in any language by systematically searching MEDLINE from 1966 to February 2007 and by manually examining the references of the original articles.

STUDY SELECTION:
We included prospective cohort studies reporting relative risks with 95% confidence intervals for the association between magnesium intake and incidence of type 2 diabetes.

RESULTS:
The seven identified cohort studies of magnesium intake [from foods only (n = 4) or from foods and supplementscombined (n = 3)] and incidence of type 2 diabetes included 286,668 participants and 10,912 cases. All but one study found an inverse relation between magnesium intake and risk of type 2 diabetes, and in four studies the association was statistically significant. The overall relative risk for a 100 mg day(-1) increase in magnesium intake was 0.85 (95% CI, 0.79-0.92). Results were similar for intake of dietary magnesium (RR, 0.86; 95% CI, 0.77-0.95) and total magnesium (RR, 0.83; 95% CI, 0.77-0.89). There was no evidence of publication bias (P = 0.99).

CONCLUSIONS:
Magnesium intake was inversely associated with incidence of type 2 diabetes. This finding suggests that increased consumption of magnesium-rich foods such as whole grains, beans, nuts, and green leafy vegetables may reduce the risk of type 2 diabetes.

Source
Larsson SC, Wolk A. Magnesium intake and risk of type 2 diabetes: a meta-analysis. J Intern Med. 2007 Aug;262(2):208-14.

Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial

ABSTRACT
BACKGROUND:
A suboptimal vitamin D and calcium status has been associated with higher risk of type 2 diabetes in observational studies, but evidence from trials is lacking.

OBJECTIVE:
We determined whether vitamin D supplementation, with or without calcium, improved glucose homeostasis in adults at high risk of diabetes.

DESIGN:
Ninety-two adults were randomly assigned in a 2-by-2 factorial-design, double-masked, placebo-controlled trial to receive either cholecalciferol (2000 IU once daily) or calcium carbonate (400 mg twice daily) for 16 wk. The primary outcome was the change in pancreatic β cell function as measured by the disposition index after an intravenous-glucose-tolerance test. Other outcomes were acute insulin response, insulin sensitivity, and measures of glycemia.

RESULTS:
Participants had a mean age of 57 y, a body mass index (BMI; in kg/m(2)) of 32, and glycated hemoglobin (Hb A(1c)) of 5.9%. There was no significant vitamin D × calcium interaction on any outcomes. The disposition index increased in the vitamin D group and decreased in the no-vitamin D group (adjusted mean change ± SE: 300 ± 130 compared with -126 ± 127, respectively; P = 0.011), which was explained by an improvement in insulin secretion (62 ± 39 compared with -36 ± 37 mU · L(-1) · min, respectively; P = 0.046). Hb A(1c) increased less, but nonsignificantly, in the vitamin D group than in the no-vitamin D group (0.06 ± 0.03% compared with 0.14 ± 0.03%, respectively; P = 0.081). There was no significant difference in any outcomes with calcium compared with no calcium.

CONCLUSION:
In adults at risk of type 2 diabetes, short-term supplementation with cholecalciferol improved β cell function and had a marginal effect on attenuating the rise in Hb A(1c).

Source
Mitri J et al. Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. Am J

Calcium and vitamin D supplementation is associated with decreased abdominal visceral adipose tissue in overweight and obese adults

ABSTRACT
BACKGROUND:
Several studies suggest that calcium and vitamin D (CaD) may play a role in the regulation of abdominal fat mass.

OBJECTIVE:
This study investigated the effect of CaD-supplemented orange juice (OJ) on weight loss and reduction of visceral adipose tissue (VAT) in overweight and obese adults (mean ± SD age: 40.0 ± 12.9 y).

DESIGN:
Two parallel, double-blind, placebo-controlled trials were conducted with either regular or reduced-energy (lite) orange juice. For each 16-wk trial, 171 participants were randomly assigned to 1 of 2 groups. The treatment groups consumed three 240-mL glasses of OJ (regular or lite) fortified with 350 mg Ca and 100 IU vitamin D per serving, and the control groups consumed either unfortified regular or lite OJ. Computed tomography scans of VAT and subcutaneous adipose tissue were performed by imaging a single cut at the lumbar 4 level.

RESULTS:
After 16 wk, the average weight loss (2.45 kg) did not differ significantly between groups. In the regular OJ trial, the reduction of VAT was significantly greater (P = 0.024) in the CaD group (-12.7 ± 25.0 cm(2)) than in the control group (-1.3 ± 13.6 cm(2)). In the lite OJ trial, the reduction of VAT was significantly greater (P = 0.039) in the CaD group (-13.1 ± 18.4 cm(2)) than in the control group (-6.4 ± 17.5 cm(2)) after control for baseline VAT. The effect of calcium and vitamin D on VAT remained highly significant when the results of the 2 trials were combined (P = 0.007).

CONCLUSIONS:
The findings suggest that calcium and/or vitamin D supplementation contributes to a beneficial reduction of VAT. This trial is registered at clinicaltrial.gov as NCT00386672, NCT01363115.

Source
Rosenblum JL et al. Calcium and vitamin D supplementation is associated with decreased abdominal visceral adipose tissue in overweight and obese adults. Am J Clin Nutr 95:101-8, 2011.

Influence of magnesium status and magnesium intake on the blood glucose control in patients with type 2 diabetes

ABSTRACT

BACKGROUND:

This study was undertaken to assess magnesium intake and magnesium status in patients with type 2 diabetes, and to identify the parameters that best predict alterations in fasting glucose and plasma magnesium.

Methods

A cross-sectional study was carried out in patients with type 2 diabetes (n = 51; 53.6 ± 10.5 y) selected within the inclusion factors, at the University Hospital Onofre Lopes. Magnesium intake was assessed by three 24-h recalls. Urine, plasma and erythrocytes magnesium, fasting and 2-h postprandial glucose, HbA1, microalbuminuria, proteinuria, and serum and urine creatinine were measured.

RESULTS:

Mean magnesium intake (9.37 ± 1.76 mmol/d), urine magnesium (2.80 ± 1.51 mmol/d), plasma magnesium (0.71 ± 0.08 mmol/L) and erythrocyte magnesium (1.92 ± 0.23 mmol/L) levels were low. Seventy-seven percent of participants presented one or more magnesium status parameters below the cut-off points of 3.00 mmol/L for urine, 0.75 mmol/L for plasma and 1.65 mmol/L for erythrocytes. Subjects presented poor blood glucose control with fasting glucose of 8.1 ± 3.7 mmol/L, 2-h postprandial glucose of 11.1 ± 5.1 mmol/L, and HbA1 of 11.4 ± 3.0%. The parameters that influenced fasting glucose were urine, plasma and dietary magnesium, while plasma magnesium was influenced by creatinine clearance.

CONCLUSIONS:

Magnesium status was influenced by kidney depuration and was altered in patients with type 2 diabetes, and magnesium showed to play an important role in blood glucose control.

Source

Sales CH, et al. Influence of magnesium status and magnesium intake on the blood glucose control in patients with type 2 diabetes. Clin Nutr. 2011 Jan 31. [Epub ahead of print]

Hypomagnesemia and diabetes mellitus. A review of clinical implications

ABSTRACT

Hypomagnesemia has long been known to be associated with diabetes mellitus. Mather et al confirmed the presence of hypomagnesemia in nearly 25% of their diabetic out-patients. Low serum magnesium level has been reported in children with insulin-dependent diabetes and through the entire spectrum of adult type I and type II diabetics regardless of the type of therapy. Hypomagnesemia has been correlated with both poor diabetic control and insulin resistance in nondiabetic elderly patients.

Source

Tosiello L, et al. Hypomagnesemia and diabetes mellitus. A review of clinical implications. Arch Intern Med 1996;156:1143-8.

BONE AND JOINT HEALTH

Patient level pooled analysis of 68 500 patients from seven major vitamin D fracture trials in US and Europe

ABSTRACT

OBJECTIVES:

To identify participants' characteristics that influence the anti-fracture efficacy of vitamin D or vitamin D plus calcium with respect to any fracture, hip fracture, and clinical vertebral fracture and to assess the influence of dosing regimens and co-administration of calcium.

DESIGN

Individual patient data analysis using pooled **DATA FROM RANDOMISED TRIALS.**

DATA SOURCES:

Seven major randomised trials of vitamin D with calcium or vitamin D alone, yielding a total of 68517 participants (mean age 69.9 years, range 47-107 years, 14.7% men).

STUDY SELECTION:

Studies included were randomised studies with at least one intervention arm in which vitamin D was given, fracture as an outcome, and at least 1000 participants.

DATA SYNTHESIS:

Logistic regression analysis was used to identify significant interaction terms, followed by Cox's proportional hazards models incorporating age, sex, fracture history, and hormone therapy and bisphosphonate use.

RESULTS:

Trials using vitamin D with calcium showed a reduced overall risk of fracture (hazard ratio 0.92, 95% confidence interval 0.86 to 0.99, P=0.025) and hip fracture (all studies: 0.84, 0.70 to 1.01, P=0.07; studies using 10 µg of vitamin D given with calcium: 0.74, 0.60 to 0.91, P=0.005). For vitamin D alone in daily doses of 10 µg or 20 µg, no significant effects were found. No interaction was found between fracture history and treatment response, nor any interaction with age, sex, or hormone replacement therapy.

CONCLUSION:

This individual patient data analysis indicates that vitamin D given alone in doses of 10-20 µg is not effective in preventing fractures. By contrast, calcium and vitamin D given together reduce hip fractures and total fractures, and probably vertebral fractures, irrespective of age, sex, or previous fractures.

Source

Abrahamsen B, et al. Patient level pooled analysis of 68 500 patients from seven major vitamin D fracture trials in US and Europe. DIPART (Vitamin D Individual Patient Analysis of Randomized Trials) Group. BMJ. 2010 Jan 12;340:b5463.

High prevalence of vitamin D insufficiency in black and white pregnant women residing in the Northern United States and their neonates

ABSTRACT
In utero or early-life vitamin D deficiency is associated with skeletal problems, type 1 diabetes, and schizophrenia, but the prevalence of vitamin D deficiency in U.S. pregnant women is unexplored. We sought to assess vitamin D status of pregnant women and their neonates residing in Pittsburgh by race and season. Serum 25-hydroxyvitamin D (25(OH)D) was measured at 4-21 wk gestation and predelivery in 200 white and 200 black pregnant women and in cord blood of their neonates. Over 90% of women used prenatal vitamins. Women and neonates were classified as vitamin D deficient [25(OH)D<37.5 nmol/L], insufficient [25(OH)D 37.5-80 nmol/L], or sufficient [25(OH)D>80 nmol/L]. At delivery, vitamin D deficiency and insufficiency occurred in 29.2% and 54.1% of black women and 45.6% and 46.8% black neonates, respectively. Five percent and 42.1% of white women and 9.7% and 56.4% of white neonates were vitamin D deficient and insufficient, respectively. Results were similar at <22 wk gestation. After adjustment for prepregnancy BMI and periconceptional multivitamin use, black women had a smaller mean increase in maternal 25(OH)D compared with white women from winter to summer (16.0+/-3.3 nmol/L vs. 23.2+/-3.7 nmol/L) and from spring to summer (13.2+/-3.0 nmol/L vs. 27.6+/-4.7 nmol/L) (P<0.01). These results suggest that black and white pregnant women and neonates residing in the northern US are at high risk of vitamin D insufficiency, even when mothers are compliant with prenatal vitamins. Higher-dose supplementation is needed to improve maternal and neonatal vitamin D nutriture.

Source
Bodnar et al. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the Northern United States and their neonates. J Nutr 2007;137:447-52.

A randomized controlled study of effects of dietary magnesium oxide supplementation on bone mineral content in healthy girls

ABSTRACT
CONTEXT:
The role of magnesium (Mg) as a determinant of bone mass has not been extensively explored. Limited studies suggest that dietary Mg intake and bone mineral density are correlated in adults, but no data from interventional studies in children and adolescents are available.

OBJECTIVE:
We sought to determine whether Mg supplementation in periadolescent girls enhances accrual of bone mass.

DESIGN:
We carried out a prospective, placebo-controlled, randomized, one-year double-blind trial of Mg supplementation.

SETTING:
The study was conducted in the Clinical Research Centers at Yale University School of Medicine.

PATIENTS OR OTHER PARTICIPANTS:
Healthy 8- to 14-yr-old Caucasian girls were recruited from community pediatricians' offices. Dietary diaries from over 120 volunteers were analyzed, and those with dietary Mg intake of less than 220 mg/d were invited to participate in the intervention.

INTERVENTION:
Magnesium (300 mg elemental Mg per day in two divided doses) or placebo was given orally for 12 months.

MAIN OUTCOME MEASURE:
The primary outcome measure was interval change in bone mineral content (BMC) of the total hip, femoral neck, Ward's area, and lumbar spine (L1-L4) after 12 months of Mg supplementation.

RESULTS:
Significantly increased accrual (P = 0.05) in integrated hip BMC occurred in the Mg-supplemented vs. placebo group. Trends for a positive Mg effect were evident in the pre- and early puberty and in mid-late puberty. Lumbar spinal BMC accrual was slightly (but not significantly) greater in the Mg-treated group. Compliance was excellent; 73% of capsules were ingested as inferred by pill counts. Serum mineral levels, calciotropic hormones, and bone markers were similar between groups.

CONCLUSIONS:
Oral Mg oxide capsules are safe and well tolerated. A positive effect of Mg supplementation on integrated hip BMC was evident in this small cohort.

Source
Carpenter TO, et al. A randomized controlled study of effects of dietary magnesium oxide supplementation on bone mineral content in healthy girls. J Clin Endocrinol Metab. 2006 Dec;91(12):4866-72.

A Multi-nutrient supplement reduced markers of inflammation and improved physical performance in active individuals of middle to older age: a randomized, double-blind, placebo-controlled study

ABSTRACT
BACKGROUND:
While exercise acts to combat inflammation and aging, the ability to exercise may itself be compromised by inflammation and inflammation's impact on muscle recovery and joint inflammation. A number of nutritional supplements have been shown to reduce inflammation and improve recovery. The purpose of the current investigation was to examine the effect of a multi-nutrient supplement containing branched chain amino acids, taurine, anti-inflammatory plant extracts, and B vitamins on inflammatory status, endothelial function, physical function, and mood in middle-aged individuals.

METHODS
Thirty-one healthy and active men (N = 16, mean age 56 ± 6.0 yrs) and women (N = 15, mean age = 52 ± 7.5 yrs) participated in this investigation. Subjects completed one 28 day cycle of placebo supplementation and one 28 day cycle of multi-nutrient supplementation (separated by a one week washout period) in a balanced, randomized,

double-blind, cross-over design. Subjects completed weekly perceptual logs (PROMIS-57, KOOS) and pre- and post-testing around the supplementation period. Testing consisted of brachial artery flow mediated dilation (FMD), blood measures, and physical performance on vertical jump, handgrip strength, and balance (dispersion from center of pressure). Significance for the investigation was $p \leq 0.05$.

RESULTS:
IL-6 significantly decreased in both men (from 1.2 ± 0.2 to 0.7 ± 0.4 pg·mL-1) and women (from 1.16 ± 0.04 to 0.7 ± 0.4 pg·mL-1). Perceived energy also improved for both men (placebo: 1.8 ± 0.7; supplement: 3.7 ± 0.8 AUC) and women (placebo: 1.2 ± 0.7; supplement: 2.8 ± 0.8 AUC). Alpha-1-antichymotrypsin (from 108.9 ± 38.6 to 55.5 ± 22.2 ug·mL-1), Creatine Kinase (from 96 ± 34 to 67 ± 23 IU·L-1), general pain, and joint pain decreased in men only, while anxiety and balance (from 0.52 ± 0.13 to 0.45 ± 0.12 cm) improved in women only. Men showed increased performance in vertical jump power (from 2642 ± 244 to 3134 ± 282 W) and grip strength (from 42.1 ± 5.9 to 48.5 ± 4.9 kg).

CONCLUSIONS:
A multi-nutrient supplement is effective in improving inflammatory status in both men and women, markers of pain, joint pain, strength, and power in men only, and both anxiety and balance (a risk factor for hip fracture) in women. Therefore, a multi-nutrient supplement may help middle-aged individuals to prolong physical function and maintain a healthy, active lifestyle.

Source
Dunn-Lewis C et al. A Multi-nutrient supplement reduced markers of inflammation and improved physical performance in active individuals of middle to older age: a randomized, double-blind, placebo-controlled study. Nutr J 10:90, 2011.

Calcium and vitamin-D supplementation on bone structural properties in peripubertal female identical twins: a randomized controlled trial

ABSTRACT

A randomised controlled trial was used in assessing the impact of 6 months of daily calcium and vitamin-D supplementation on trabecular and cortical bone acquisition at distal tibial and radial sites using peripheral quantitative computed tomography (pQCT). Daily supplementation was associated with increased bone density and bone strength at the distal tibia and radius.

INTRODUCTION:
pQCT has not been used to assess bone responses to calcium and vitamin-D supplementation on peripubertal children. This randomised controlled trial aimed to assess the impact of a 6-month daily calcium and vitamin-D supplementation on trabecular and cortical bone acquisition at distal tibial and radial sites using pQCT.

METHODS:
Twenty pairs of peripubertal female identical twins, aged 9 to 13 years, were randomly assigned to receive either 800 mg of calcium and 400 IU of vitamin D3, or a matched placebo. Bone structural properties at the distal tibia and distal radius were acquired at baseline and 6 months.

RESULTS:
The calcium-supplemented group showed greater gains in trabecular density, trabecular area and strength strain index at the 4% of distal tibial and radial sites compared with the placebo group (p=0.001). Greater gains in cortical area at the 38% and 66% of tibial sites were also found in twins receiving the calcium supplement (p=0.001).

CONCLUSIONS:
Daily supplementation for a period of 6 months was associated with increased trabecular area, trabecular density and strength strain index at the ultra-distal tibia and radius and increased cortical area at tibial mid-shaft.

Source
Greene DA, et al. Calcium and vitamin-D supplementation on bone structural properties in peripubertal female identical twins: a randomized controlled trial. osteoporos Int. 2011 Feb;22(2):489-98. Epub 2010 Jun 11.

Effect of glucosamine sulfate with or without omega-3 fatty acids in patients with osteoarthritis

ABSTRACT

INTRODUCTION:
A total of 177 patients with moderate-to-severe hip or knee osteoarthritis (OA) were tested over a period of 26 weeks in a two-center, two-armed, randomized, double-blind, comparison study. The aim was to see if a combination of glucosamine sulfate (1500 mg/day) and the omega-3 polyunsaturated fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (group A), showed equivalence (noninferiority) or superiority as opposed to glucosamine sulfate alone (group B).

METHODS:
The primary therapy evaluation was performed using the Western Ontario and McMaster Universities Arthrosis index (WOMAC) score. At the end of the study, a reduction in the pain score of > or =20% was required (primary target criterion) and the quantitative difference in the WOMAC subscores pain, stiffness, and function were analyzed (secondary target criteria).

RESULTS AND CONCLUSION:
When a minimal pain reduction of > or =20% was chosen, there was no statistically significant difference in the number of responders between the two groups (92.2% group A, 94.3% group B). A higher responder criterion (> or =80% reduction in the WOMAC pain score) was chosen. Therefore, the frequency of responders showed a therapeutic and statistical superiority for the combination product of glucosamine sulfate and the omega-3 polyunsaturated fatty acids in patients who complied with the study protocol (group A 44%, group B 32%; P=0.044). OA symptoms (morning stiffness, pain in hips and knees) were reduced at the end of the study: by 48.5%-55.6% in group A and by 41.7%-55.3% in group B. The reduction was greater in group A than in group B. There was a tendency toward superiority shown in the secondary target criteria and concurrent variables. In the global safety evaluation, both products have been demonstrated to be very safe in long-term treatment over 26 weeks. To our knowledge, this is the first clinical trial in which glucosamine was given in combination with omega-3 fatty acids to patients with OA.

Source
Gruenwald J, et al. Effect of glucosamine sulfate with or without omega-3 fatty acids in patients with osteoarthritis. Adv Ther. 2009 Sep;26(9):858-71.

Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease

ABSTRACT
Most humans depend on sun exposure to satisfy their requirements for vitamin D. Solar ultraviolet B photons are absorbed by 7-dehydrocholesterol in the skin, leading to its transformation to previtamin D3, which is rapidly converted to vitamin D3. Season, latitude, time of day, skin pigmentation, aging, sunscreen use, and glass all influence the cutaneous production of vitamin D3. Once formed, vitamin D3 is metabolized in the liver to 25-hydroxyvitamin D3 and then in the kidney to its biologically active form, 1,25-dihydroxyvitamin D3. Vitamin D deficiency is an unrecognized epidemic among both children and adults in the United States. Vitamin D deficiency not only causes rickets among children but also precipitates and exacerbates osteoporosis among adults and causes the painful bone disease osteomalacia. Vitamin D deficiency has been associated with increased risks of deadly cancers, cardiovascular disease, multiple sclerosis, rheumatoid arthritis, and type 1 diabetes mellitus. Maintaining blood concentrations of 25-hydroxyvitamin D above 80 nmol/L (approximately 30 ng/mL) not only is important for maximizing intestinal calcium absorption but also may be important for providing the extrarenal 1alpha-hydroxylase that is present in most tissues to produce 1,25-dihydroxyvitamin D3. Although chronic excessive exposure to sunlight increases the risk of nonmelanoma skin cancer, the avoidance of all direct sun exposure increases the risk of vitamin D deficiency, which can have serious consequences. Monitoring serum 25-hydroxyvitamin D concentrations yearly should help reveal vitamin D deficiencies. Sensible sun exposure (usually 5-10 min of exposure of the arms and legs or the hands, arms, and face, 2 or 3 times per week) and increased dietary and supplemental vitamin D intakes are reasonable approaches to guarantee vitamin D sufficiency.

Source
Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr. 2004 Dec;80(6 Suppl):1678S-88S.

Inflammatory cells during wound repair: the good, the bad and the ugly

ABSTRACT
Damage to any tissue triggers a cascade of events that leads to rapid repair of the wound - if the tissue is skin, then repair involves re-epithelialization, formation of granulation tissue and contraction of underlying wound connective tissues. This concerted effort by the wounded cell layers is accompanied by, and might also be partially regulated by, a robust inflammatory response, in which first neutrophils and then macrophages and mast cells emigrate from nearby tissues and from the circulation. Clearly, this inflammatory response is crucial for fighting infection and must have been selected for during the course of evolution so that tissue damage did not inevitably lead to death through septicemia. But, aside from this role, exactly what are the functions of the various leukocyte lineages that are recruited with overlapping time courses to the wound site, and might they do more harm than good? Recent knockout and knockdown studies suggest that depletion of one or more of the inflammatory cell lineages can even enhance healing, and we discuss new views on how regulation of the migration of inflammatory cells to sites of tissue damage might guide therapeutic strategies for modulating the inflammatory response.

Source
Martin P, et al. Inflammatory cells during wound repair: the good, the bad and the ugly. Trends Cell Biol. 2005 Nov;15(11):599-607.

Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial

ABSTRACT
BACKGROUND:
A suboptimal vitamin D and calcium status has been associated with higher risk of type 2 diabetes in observational studies, but evidence from trials is lacking.

OBJECTIVE:
We determined whether vitamin D supplementation, with or without calcium, improved glucose homeostasis in adults at high risk of diabetes.

DESIGN:
Ninety-two adults were randomly assigned in a 2-by-2 factorial-design, double-masked, placebo-controlled trial to receive either cholecalciferol (2000 IU once daily) or calcium carbonate (400 mg twice daily) for 16 wk. The primary outcome was the change in pancreatic β cell function as measured by the disposition index after an intravenous-glucose-tolerance test. Other outcomes were acute insulin response, insulin sensitivity, and measures of glycemia.

RESULTS:
Participants had a mean age of 57 y, a body mass index (BMI; in kg/m(2)) of 32, and glycated hemoglobin (Hb A(1c)) of 5.9%. There was no significant vitamin D × calcium interaction on any outcomes. The disposition index increased in the vitamin D group and decreased in the no-vitamin D group (adjusted mean change ± SE: 300 ± 130 compared with -126 ± 127, respectively; P = 0.011), which was explained by an improvement in

insulin secretion (62 ± 39 compared with -36 ± 37 mU · L(-1) · min, respectively; P = 0.046). Hb A(1c) increased less, but nonsignificantly, in the vitamin D group than in the no-vitamin D group (0.06 ± 0.03% compared with 0.14 ± 0.03%, respectively; P = 0.081). There was no significant difference in any outcomes with calcium compared with no calcium.

CONCLUSION:
In adults at risk of type 2 diabetes, short-term supplementation with cholecalciferol improved β cell function and had a marginal effect on attenuating the rise in Hb A(1c).

Source
Mitri J et al. Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. Am J

Magnesium intake from food and supplements is associated with bone mineral density in healthy older white subjects

ABSTRACT
OBJECTIVES:
To determine whether magnesium intake from supplemental and dietary sources is associated with bone mineral density (BMD) in older men and women.

DESIGN:
Cross-sectional.

SETTING:
Memphis, Tennessee, and Pittsburgh, Pennsylvania.

PARTICIPANTS:
Two thousand thirty-eight older black and white men and women aged 70 to 79 at baseline enrolled in the Health, Aging and Body Composition Study.

MEASUREMENTS:
Dietary intake of magnesium was assessed using a semiquantitative food frequency questionnaire, and supplement data were collected based on a medication inventory. BMD of the whole body was obtained using a fan-beam densitometer. Additional covariates included age, body mass index (BMI), smoking status, alcohol use, physical activity, estrogen use, and supplemental calcium (Ca) and vitamin D use.

RESULTS:
In white, but not black, men and women, magnesium intake was positively associated with BMD of the whole body after adjustment for age, self-report of osteoporosis or fracture in adulthood, caloric intake, Ca and vitamin D intake, BMI, smoking status, alcohol intake, physical activity, thiazide diuretic use, and estrogen use in women (P=.05 for men and P=.005 for women). BMD was 0.04 g/cm2 higher in white women and 0.02 g/cm2 higher in white men in the highest than in the lowest quintile of magnesium intake.

CONCLUSION:
Greater magnesium intake was significantly related to higher BMD in white women and men. The lack of association observed in black women and men may be related to differences in Ca regulation or in nutrient reporting.

Source
Ryder KM,et al.Magnesium intake from food and supplements is associated with bone mineral density in healthy older white subjects. J Am Geriatr Soc. 2005 Nov;53(11):1875-80.

Calcium and vitamin D supplementation through fortified dairy products counterbalances seasonal variations of bone metabolism indices: the Postmenopausal Health Study

ABSTRACT
PURPOSE:
To assess the effectiveness of a dietary intervention combined with fortified dairy products on bone metabolism and bone mass indices in postmenopausal women.

METHODS:
Forty postmenopausal women (55-65 years old) were equally randomized into a dietary group (DG), receiving daily and for 30 months, 1,200 mg of calcium and 7.5 µg of vitamin D(3) for the first 12 months that increased to 22.5 µg for the remaining 18 months of intervention through fortified dairy products; and a control group (CG). Differences in the changes of bone metabolism and bone mass indices were examined with repeated measures ANOVA.

RESULTS:
A significant increase was observed for PTH levels only in the CG during the first six winter months of intervention (p = 0.049). After 30 months of intervention, during winter, serum 25(OH)D significantly decreased in the CG while remained in the same high levels as in the summer period in the DG. Serum RANKL levels decreased significantly in the DG compared with the increase in the CG during the 30-month intervention period (p = 0.005). Serum CTx decreased significantly in the DG after six (-0.08; -0.12 to -0.03) and 12 (-0.03; -0.08 to -0.02) months of intervention. Finally, the DG had more favorable changes in total body BMD than the CG (p < 0.001).

CONCLUSIONS:
Increasing dietary intake of calcium and vitamin D in osteopenic postmenopausal women appears to be effective in producing favorable changes in several bone metabolism and bone mass indices and in counterbalancing seasonal variations in hormonal and biochemical molecules.

Source
Tenta R, et al. Calcium and vitamin D supplementation through fortified dairy products counterbalances seasonal variations of bone metabolism indices: the Postmenopausal Health Study. Eur J Nutr. 2010 Dec 14. [Epub ahead of print]

BREAST HEALTH

Circulating Carotenoids and Risk of Breast Cancer: Pooled Analysis of Eight Prospective Studies

ABSTRACT

BACKGROUND:

Carotenoids, micronutrients in fruits and vegetables, may reduce breast cancer risk. Most, but not all, past studies of circulating carotenoids and breast cancer have found an inverse association with at least one carotenoid, although the specific carotenoid has varied across studies.

METHODS:

We conducted a pooled analysis of eight cohort studies comprising more than 80% of the world's published prospective data on plasma or serum carotenoids and breast cancer, including 3055 case subjects and 3956 matched control subjects. To account for laboratory differences and examine population differences across studies, we recalibrated participant carotenoid levels to a common standard by reassaying 20 plasma or serum samples from each cohort together at the same laboratory. Using conditional logistic regression, adjusting for several breast cancer risk factors, we calculated relative risks (RRs) and 95% confidence intervals (CIs) using quintiles defined among the control subjects from all studies. All P values are two-sided.

RESULTS:

Statistically significant inverse associations with breast cancer were observed for α-carotene (top vs bottom quintile RR = 0.87, 95% CI = 0.71 to 1.05, P(trend) = .04), β-carotene (RR = 0.83, 95% CI = 0.70 to 0.98, P(trend) = .02), lutein+zeaxanthin (RR = 0.84, 95% CI = 0.70 to 1.01, P(trend) = .05), lycopene (RR = 0.78, 95% CI = 0.62 to 0.99, P(trend) = .02), and total carotenoids (RR = 0.81, 95% CI = 0.68 to 0.96, P(trend) = .01). β-Cryptoxanthin was not statistically significantly associated with risk. Tests for heterogeneity across studies were not statistically significant. For several carotenoids, associations appeared stronger for estrogen receptor negative (ER(-)) than for ER(+) tumors (eg, β-carotene: ER(-): top vs bottom quintile RR = 0.52, 95% CI = 0.36 to 0.77, P(trend) = .001; ER(+): RR = 0.83, 95% CI = 0.66 to 1.04, P(trend) = .06; P(heterogeneity) = .01).

CONCLUSIONS:

This comprehensive prospective analysis suggests women with higher circulating levels of α-carotene, β-carotene, lutein+zeaxanthin, lycopene, and total carotenoids may be at reduced risk of breast cancer.

Source

Eliassen AH, et al. Circulating Carotenoids and Risk of Breast Cancer: Pooled Analysis of Eight Prospective Studies. J Natl Cancer Inst. 2012 Dec 19;104(24):1905-16

CELLULAR HEALTH

Protective role of 1 alpha, 25-dihydroxyvitamin D3 against oxidative stress in nonmalignant human prostate epithelial cells

ABSTRACT

Overproduction of reactive oxygen species (ROS), through either endogenous or exogenous sources, could induce DNA damage, and accumulation of DNA damage might lead to multistep carcinogenesis. The antioxidative effects of vitamin D have been suggested by epidemiological and many in vitro and in vivo laboratory studies. While exploring the antioxidative effects of vitamin D in prostate cells, we found that the active form of vitamin D, 1 alpha, 25-dihydroxyvitamin D(3) (1,25-VD), can protect nonmalignant human prostate epithelial cell lines, BPH-1 and RWPE-1, but not malignant human prostate epithelial cells, CWR22R and DU 145, from oxidative stress-induced cell death. Glucose-6-phosphate dehydrogenase (G6PD), a key antioxidant enzyme, was dose- and time-dependently induced by 1,25-VD. Mechanistic studies using chromatin immunoprecipitation (ChIP) assay revealed that a direct repeat-3 (DR3) vitamin D response element located in the first intron of the G6PD genome can be bound by liganded vitamin D receptor, thereby regulating G6PD gene expression. Increasing G6PD activity and glutathione level by 1,25-VD can scavenge cellular ROS. Moreover, the protective effects of 1,25-VD were abolished by dehydroepiandrosterone, a non-competitive inhibitor of G6PD activity. Together, our results showed that 1,25-VD can protect nonmalignant prostate cells from oxidative stress-induced cell death by elimination of ROS-induced cellular injuries through transcriptional activation of G6PD activity. The antioxidative effect of vitamin D strengthens its roles in cancer chemoprevention and adds to a growing list of beneficial effects of vitamin D against cancer.

Source

Bao BY, et al. Protective role of 1 alpha, 25-dihydroxyvitamin D3 against oxidative stress in nonmalignant human prostate epithelial cells. Int J Cancer. 2008 Jun 15;122(12):2699-706

Recent advances in clinical research involving carotenoids

ABSTRACT

Epidemiological studies show consistent decreased risk of lung cancer and certain other cancers, cataracts, age-related macular degeneration, and coronary heart disease in populations with the highest intakes of carotenoid-rich diets. Intervention studies show reductions in precancerous oral lesions, enhancement in immune parameters, and reduced incidence of cardiovascular events in individuals supplemented with β-carotene.

Source

Bendich A, et al. Recent advances in clinical research involving carotenoids. Pure & Appl Chem. 1994;66(5): 1017-1024.

Physicians and nurses use and recommend dietary supplements: report of a survey

ABSTRACT

BACKGROUND:

Numerous surveys show that dietary supplements are used by a large proportion of

the general public, but there have been relatively few surveys on the prevalence of dietary supplement use among health professionals, including physicians and nurses. Even less information is available regarding the extent to which physicians and nurses recommend dietary supplements to their patients.

METHODS:
An online survey was administered in October 2007 to 900 physicians and 277 nurses by Ipsos Public Affairs for the Council for Responsible Nutrition (CRN), a trade association representing the dietary supplement industry. The health professionals were asked whether they used dietary supplements and their reasons for doing so, and whether they recommend dietary supplements to their patients.

RESULTS:
The "Life...supplemented" Healthcare Professionals Impact Study (HCP Impact Study) found that 72% of physicians and 89% of nurses in this sample used dietary supplements regularly, occasionally, or seasonally. Regular use of dietary supplements was reported by 51% of physicians and 59% of nurses. The most common reason given for using dietary supplements was for overall health and wellness (40% of physicians and 48% of nurses), but more than two-thirds cited more than one reason for using the products. When asked whether they "ever recommend dietary supplements" to their patients, 79% of physicians and 82% of nurses said they did.

CONCLUSION:
Physicians and nurses are as likely as members of the general public to use dietary supplements, as shown by comparing the results of this survey with data from national health and nutrition surveys. Also, most physicians and nurses recommend supplements to their patients, whether or not the clinicians use dietary supplements themselves.

Source
Dickinson A, et al. Physicians and nurses use and recommend dietary supplements: report of a survey. Nutr J. 2009 Jul 1;8:29.

Effect of low carotene diet on malondialdehyde (MDA) concentration

ABSTRACT
OBJECTIVE:
The purpose of the study was to evaluate the effect of a low carotenoid diet (83 micrograms Beta-carotene) on malondialdehyde-thiobarbituric acid (MDA-TBA) concentrations of nine pre-menopausal women.

METHODS:
Subjects lived on the metabolic research unit of the Western Human Nutrition Research Center (WHNRC), where diet, exercise and other activities were controlled. Five subjects (Group C, control group) consumed a low carotenoid diet and received an additional 0.5 mg/day of Beta-carotene while four subjects (Group P, placebo group) received only the low carotenoid diet during days 1 to 60 (period 1). All subjects received 0.5 mg/day of Beta-carotene during days 60 to 100 (period 2), plus three capsules/day mixed carotenoid supplement (Neo-Life Company) during study days 100 to 120. Changes in MDA-TBA concentrations were analyzed during the study periods and between the groups.

RESULTS:
At the start of the study (day 1), no significant difference in the MDA-TBA concentration was observed between the control (Group C) and the placebo (Group P) subjects. During period 1 (days 2 to 60), when Group P subjects consumed the low carotenoid diet without supplementation, the MDA-TBA values for Group P rose markedly and were significantly ($p < 0.05$) higher than the MDA-TBA values for Group C subjects who were receiving carotenoid supplementation. During period 2 (days 60 to 100) when both groups received carotenoid supplementation, the MDA-TBA values of Group P subjects were significantly ($p < 0.05$) reduced to the point where they were similar to the MDA-TBA values for Group C subjects.

CONCLUSIONS:
These findings provide evidence to support the beneficial effects of carotenoids in preventing lipid peroxidation in the cells. Further studies are needed to identify the exact mechanism by which carotenoids prevent lipid peroxidation and the amount needed for normal activity.

Source
Dixon ZR, et al. Effect of low carotene diet on malondialdehyde (MDA) concentration; Free Radic Biol Med. 1996.

Effects of a carotene-deficient diet on measures of oxidative susceptibility and superoxide dismutase activity in adult women

ABSTRACT
The effect of consuming a low carotene diet (approximately 60 micrograms carotene/day) on oxidative susceptibility and superoxide dismutase (SOD) activity in women living in a metabolic research unit was evaluated. The diet had sufficient vitamins A, E, and C. The women ate the diet supplemented with 1500 micrograms/day beta-carotene for 4 days (baseline), then the unsupplemented diet for 68 days (depletion), followed by the diet supplemented with > 15,000 micrograms/day carotene for 28 days (repletion). Production of hexanal, pentanal, and pentane by copper-oxidized plasma low density lipoproteins from carotene-depleted women was greater than their production of these compounds when repleted with carotene. Erythrocyte SOD activity was depressed in carotene-depleted women; it recovered with repletion. Thiobarbituric acid reactive substances in plasma of carotene-depleted women were elevated and diminished with repletion. Dietary carotene seems to be needed, not only as a precursor of vitamin A, but also to inhibit oxidative damage and decrease oxidation susceptibility.

Source
Dixon ZR, et al. Effects of a carotene-deficient diet on measures of oxidative susceptibility and superoxide dismutase activity in adult women. Free Radic Biol Med. 1994 Dec;17(6):537-44.

Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease

ABSTRACT
Most humans depend on sun exposure to satisfy their requirements for vitamin D. Solar ultraviolet B photons are absorbed by 7-dehydrocholesterol in the skin, leading to its transformation to previtamin D3, which is rapidly converted to vitamin D3. Season, latitude, time of day, skin pigmentation, aging, sunscreen use, and glass all influence the cutaneous production of vitamin D3. Once formed, vitamin D3 is metabolized in the liver to 25-hydroxyvitamin D3 and then in the kidney to its biologically active form, 1,25-dihydroxyvitamin D3. Vitamin D deficiency is an unrecognized epidemic among both children and adults in the United States. Vitamin D deficiency not only causes rickets among children but also precipitates and exacerbates osteoporosis among adults and causes the painful bone disease osteomalacia. Vitamin D deficiency has been associated with increased risks of deadly cancers, cardiovascular disease, multiple sclerosis, rheumatoid arthritis, and type 1 diabetes mellitus. Maintaining blood concentrations of 25-hydroxyvitamin D above 80 nmol/L (approximately 30 ng/mL) not only is important for maximizing intestinal calcium absorption but also may be important for providing the extrarenal 1alpha-hydroxylase that is present in most tissues to produce 1,25-dihydroxyvitamin D3. Although chronic excessive exposure to sunlight increases the risk of nonmelanoma skin cancer, the avoidance of all direct sun exposure increases the risk of vitamin D deficiency, which can have serious consequences. Monitoring serum 25-hydroxyvitamin D concentrations yearly should help reveal vitamin D deficiencies. Sensible sun exposure (usually 5-10 min of exposure of the arms and legs or the hands, arms, and face, 2 or 3 times per week) and increased dietary and supplemental vitamin D intakes are reasonable approaches to guarantee vitamin D sufficiency.

Source
Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr. 2004 Dec;80(6 Suppl):1678S-88S.

Docosapentaenoic acid (22:5n-3): a review of its biological effects.

ABSTRACT
This article summarizes the current knowledge available on metabolism and the biological effects of n-3 docosapentaenoic acid (DPA). n-3 DPA has not been extensively studied because of the limited availability of the pure compound. n-3 DPA is an elongated metabolite of EPA and is an intermediary product between EPA and DHA. The literature on n-3 DPA is limited, however the available data suggests it has beneficial health effects. In vitro n-3 DPA is retro-converted back to EPA, however it does not appear to be readily metabolised to DHA. In vivo studies have shown limited conversion of n-3 DPA to DHA, mainly in liver, but in addition retro-conversion to EPA is evident in a number of tissues. n-3 DPA can be metabolised by lipoxygenase, in platelets, to form ll-hydroxy-7,9,13,16,19- and 14-hydroxy-7,10,12,16,19-DPA. It has also been reported that n-3 DPA is effective (more so than EPA and DHA) in inhibition of aggregation in platelets obtained from rabbit blood. In addition, there is evidence that n-3 DPA possesses 10-fold greater endothelial cell migration ability than EPA, which is important in wound-healing processes. An in vivo study has reported that n-3 DPA reduces the fatty acid synthase and malic enzyme activity levels in n-3 DPA-supplemented mice and these effects were stronger than the EPA-supplemented mice. Another recent in vivo study has reported that n-3 DPA may have a role in attenuating age-related decrease in spatial learning and long-term potentiation. However, more research remains to be done to further investigate the biological effects of this n-3 VLCPUFA.

Source
Kaur G, et al. Docosapentaenoic acid (22:5n-3): a review of its biological effects. Progressive Lipid Research. 2011 Jan; 50(1):28-34

Serum α-carotene concentrations and risk of death among US Adults: the Third National Health and Nutrition Examination Survey Follow-up Study

ABSTRACT
BACKGROUND:
Much research has been conducted relating total carotenoids--and β-carotene in particular--to risk of cancer and cardiovascular disease (CVD). Limited data are emerging to implicate the important role of α-carotene in the development of CVD or cancer.

METHODS:
We assessed the direct relationship between α-carotene concentrations and risk of death among 15,318 US adults 20 years and older who participated in the Third National Health and Nutrition Examination Survey Follow-up Study. We used Cox proportional hazard regression analyses to estimate the relative risk for death from all causes and selected causes associated with serum α-carotene concentrations.

RESULTS:
Compared with participants with serum α-carotene concentrations of 0 to 1 μg/dL (to convert to micromoles per liter, multiply by 0.01863), those with higher serum levels had a lower risk of death from all causes (P < .001 for linear trend): the relative risk for death was 0.77 (95% confidence interval, 0.68-0.87) among those with α-carotene concentrations of 2 to 3 μg/dL, 0.73 (0.65-0.83) among those with concentrations of 4 to 5 μg/dL, 0.66 (0.55-0.79) among those with concentrations of 6 to 8 μg/dL, and 0.61 (0.51-0.73) among those with concentrations of 9 μg/dL or higher after adjustment for potential confounding variables. We also found significant associations between serum α-carotene concentrations and risk of death from CVD (P = .007), cancer (P = .02), and all other causes (P <

.001). The association between serum α-carotene concentrations and risk of death from all causes was significant in most subgroups stratified by demographic characteristics, lifestyle habits, and health risk factors.

CONCLUSIONS:
Serum α-carotene concentrations were inversely associated with risk of death from all causes, CVD, cancer, and all other causes. These findings support increasing fruit and vegetable consumption as a means of preventing premature death.

Source
Li C, et al. Serum α-carotene concentrations and risk of death among US Adults: the Third National Health and Nutrition Examination Survey Follow-up Study. Arch Intern Med. 2011 Mar 28;171(6):507-15.

Expression of the multiple sclerosis-associated MHC class II Allele HLA-DRB1*1501 is regulated by vitamin D

ABSTRACT
Multiple sclerosis (MS) is a complex trait in which allelic variation in the MHC class II region exerts the single strongest effect on genetic risk. Epidemiological data in MS provide strong evidence that environmental factors act at a population level to influence the unusual geographical distribution of this disease. Growing evidence implicates sunlight or vitamin D as a key environmental factor in aetiology. We hypothesised that this environmental candidate might interact with inherited factors and sought responsive regulatory elements in the MHC class II region. Sequence analysis localised a single MHC vitamin D response element (VDRE) to the promoter region of HLA-DRB1. Sequencing of this promoter in greater than 1,000 chromosomes from HLA-DRB1 homozygotes showed absolute conservation of this putative VDRE on HLA-DRB1*15 haplotypes. In contrast, there was striking variation among non-MS-associated haplotypes. Electrophoretic mobility shift assays showed specific recruitment of vitamin D receptor to the VDRE in the HLA-DRB1*15 promoter, confirmed by chromatin immunoprecipitation experiments using lymphoblastoid cells homozygous for HLA-DRB1*15. Transient transfection using a luciferase reporter assay showed a functional role for this VDRE. B cells transiently transfected with the HLA-DRB1*15 gene promoter showed increased expression on stimulation with 1,25-dihydroxyvitamin D3 (P = 0.002) that was lost both on deletion of the VDRE or with the homologous "VDRE" sequence found in non-MS-associated HLA-DRB1 haplotypes. Flow cytometric analysis showed a specific increase in the cell surface expression of HLA-DRB1 upon addition of vitamin D only in HLA-DRB1*15 bearing lymphoblastoid cells. This study further implicates vitamin D as a strong environmental candidate in MS by demonstrating direct functional interaction with the major locus determining genetic susceptibility. These findings support a connection between the main epidemiological and genetic features of this disease with major practical implications for studies of disease mechanism and prevention.

Source
Ramagopalan SV, et al. Expression of the multiple sclerosis-associated MHC class II Allele HLA-DRB1*1501 is regulated by vitamin D. PLoS Genet. 2009 Feb;5(2):e1000369.

Low serum 25-hydroxyvitamin D concentrations are associated with greater all-cause mortality in older community-dwelling women

ABSTRACT
Vitamin D deficiency is associated with osteoporosis, poor muscle strength, falls, and fractures. The relationship between serum vitamin D concentrations and mortality in older community-dwelling women has not been well characterized. We hypothesized that women with lower 25-hydroxyvitamin D (25[OH]D) concentrations were at higher risk of mortality. We examined the association between serum 25[OH]D concentrations and all-cause mortality in a prospective, population-based study of 714 community-dwelling women, aged 70 to 79 years, the Women's Health and Aging Studies I and II in Baltimore, Md. The studies were originally designed to evaluate the causes and course of physical disability in older women living in the community. Vital status was determined through follow-up interviews and matching with the National Death Index. During a median of 72 months of follow-up, 100 (14%) of 714 women died. Women in the lowest quartile of 25(OH)D (<15.3 ng/mL or 38.2 nmol/L) were at higher risk of death (hazards ratio, 2.45; 95% confidence interval, 1.12-5.36; P = .02) compared to women in the highest quartile (>27.0 ng/mL or 67.4 nmol/L) of 25(OH)D in a multivariate Cox proportional hazards model adjusting for demographics, season, and conventional risk factors. Older community-dwelling women with low 25(OH)D levels are at an increased risk of death.

Source
Semba R, et al. Low serum 25-hydroxyvitamin D concentrations are associated with greater all-cause mortality in older community-dwelling women. Nutr Resear. 2009 Aug;29(8):525-30

Vitamin D and chronic pain

ABSTRACT
Results:
We identified 22 relevant studies that reported mean 25-OH vitamin D levels and/or investigated the results of vitamin D treatment in patients with chronic pain conditions. Five were randomized double blind trials of vitamin D treatment [12,13,15,23,33]. Eight studies with weaker designs more prone to bias also evaluated vitamin D treatment; two were randomised but not double blind [19,32] and six were case series [2,9,11,14,21,28]. Nine purely observational studies were without treatment [3,4,7,16,18,22,26,27,30]. One study [4] reported results separately for men and women and was treated as two data sets. These 23 data sets ranged in size from 5 to

3459 patients. The total number of patients in ''pain" and ''control" groups was 8644; 58% were women. Few studies actually measured vitamin D status, and there was no common definition of what constituted deficiency.

The expected dependence of 25-OH vitamin D level on latitude was confirmed, with lower average levels at higher latitude, though with considerable variability between populations (Fig. 1).

Three observational studies explored differences in 25-OH vitamin D levels between patients with and without chronic musculoskeletal or widespread pain. Two very small studies (104 patients in total) [7,22] claimed significantly reduced 25-OH vitamin D levels in pain subjects compared with controls. In a large study [4], a significant association between 25-OH vitamin D levels and increased pain was found in only one of the several analyses for 3495 women, but not for 3365 men. Another study [33] investigated 25-OH vitamin D levels in patients with diffuse musculoskeletal pain and used patients with osteoarthritis as a ''control" group. It found no difference in 25-OH vitamin D levels between these two populations; because the control group also consisted of patients with a chronically painful condition, both groups of patients from this study are treated as ''pain" populations for the purpose of this review.

Characteristics of treatment studies are in Table 1. Vitamin D treatments involved monthly equivalent doses between 1200 and 400,000 IU. Fourteen studies were in musculoskeletal pain [2,7,11–14,16,19,22,23,27,28,32,33], five in chronic widespread pain or fibromyalgia [3,4,9,18,26], one in diabetic subjects with neuropathic pain [21], one addressing an unusual hyperaesthetic pain syndrome [14], and one with various conditions [30]. Patients in these studies may have had ill-defined subclinical or overt osteomalacia, as is not infrequently the case with vitamin D deficiency. Duration of treatment was from a few days to 12 months, though most studies lasted two months or more. It was rare for studies to report on adverse events.

Treatment studies involved 733 patients. Randomised double blind trials involved 229 patients, of whom only 22 (10%) were in a trial with a significant improvement in pain with vitamin D, and then only on a pain mobility measure; 207 patients were in trials with no significant improvement in pain with vitamin D. Only one of these randomised trials [33] measured 25-OH vitamin D, demonstrating both deficiency at baseline and significant change with treatment. By contrast, six of eight treatment studies that were not double blind showed significant improvement in pain with vitamin D (457 of 504 patients, 93%). Only three of these trials [9,11,28] measured vitamin status. There was no apparent correlation between significant improvement in pain with vitamin D and a particular preparation, dose, or condition (Table 1).

Source
Straube S, et al. Vitamin D and chronic pain. Pain. 2009 Jan;141(1-2):10-3. Epub 2008 Dec 11.

CHILDREN'S HEALTH

High prevalence of vitamin D insufficiency in black and white pregnant women residing in the Northern United States and their neonates

ABSTRACT
In utero or early-life vitamin D deficiency is associated with skeletal problems, type 1 diabetes, and schizophrenia, but the prevalence of vitamin D deficiency in U.S. pregnant women is unexplored. We sought to assess vitamin D status of pregnant women and their neonates residing in Pittsburgh by race and season. Serum 25-hydroxyvitamin D (25(OH)D) was measured at 4-21 wk gestation and predelivery in 200 white and 200 black pregnant women and in cord blood of their neonates. Over 90% of women used prenatal vitamins. Women and neonates were classified as vitamin D deficient [25(OH)D<37.5 nmol/L], insufficient [25(OH)D 37.5-80 nmol/L], or sufficient [25(OH)D>80 nmol/L]. At delivery, vitamin D deficiency and insufficiency occurred in 29.2% and 54.1% of black women and 45.6% and 46.8% black neonates, respectively. Five percent and 42.1% of white women and 9.7% and 56.4% of white neonates were vitamin D deficient and insufficient, respectively. Results were similar at <22 wk gestation. After adjustment for prepregnancy BMI and periconceptional multivitamin use, black women had a smaller mean increase in maternal 25(OH)D compared with white women from winter to summer (16.0+/-3.3 nmol/L vs. 23.2+/-3.7 nmol/L) and from spring to summer (13.2+/-3.0 nmol/L vs. 27.6+/-4.7 nmol/L) (P<0.01). These results suggest that black and white pregnant women and neonates residing in the northern US are at high risk of vitamin D insufficiency, even when mothers are compliant with prenatal vitamins. Higher-dose supplementation is needed to improve maternal and neonatal vitamin D nutriture.

Source
Bodnar et al. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the Northern United States and their neonates. J Nutr 2007;137:447-52.

Periconceptional multivitamin use and infant birth weight disparities.

ABSTRACT
PURPOSE:
In the United States, African American women deliver preterm and low birth weight infants two to three times more frequently than their white counterparts. Our objective was to determine whether maternal periconceptional multivitamin (MVI) use is associated with this disparity.

METHODS:
As a secondary analysis of previously collected data from mothers of non-malformed infants from the Slone Epidemiology Center Birth Defects Study, we conducted a retrospective cohort study of 2331 non-Hispanic white and 133 non-Hispanic black mother/infant pairs from 1998 through 2007. To estimate the effect of MVI use on birth outcomes, linear regression models were used.

RESULTS:
In white subjects, MVI use was not associ-

ated with birth weight, gestational age, or weight-for-gestational-age. However, in black subjects, MVI use was associated with a 536-gram increased birth weight (p=0.001). Black MVI users also had longer gestations (although not statistically significant). When birth weights were adjusted for gestational age using z scores, MVI use was associated with increased fetal growth in black infants (+0.86 z score units, 95% confidence interval: 0.35-1.36).

CONCLUSIONS:
The present findings suggest MVI use may improve fetal growth and possibly gestational age in the offspring of African American women.

Source
Burris HH, et al. Periconceptional multivitamin use and infant birth weight disparities. Ann Epidemiol. 2010 Mar;20(3):233-40.

A randomized controlled study of effects of dietary magnesium oxide supplementation on bone mineral content in healthy girls

ABSTRACT
CONTEXT:
The role of magnesium (Mg) as a determinant of bone mass has not been extensively explored. Limited studies suggest that dietary Mg intake and bone mineral density are correlated in adults, but no data from interventional studies in children and adolescents are available.

OBJECTIVE:
We sought to determine whether Mg supplementation in periadolescent girls enhances accrual of bone mass.

DESIGN:
We carried out a prospective, placebo-controlled, randomized, one-year double-blind trial of Mg supplementation.

SETTING:
The study was conducted in the Clinical Research Centers at Yale University School of Medicine.

PATIENTS OR OTHER PARTICIPANTS:
Healthy 8- to 14-yr-old Caucasian girls were recruited from community pediatricians' offices. Dietary diaries from over 120 volunteers were analyzed, and those with dietary Mg intake of less than 220 mg/d were invited to participate in the intervention.

INTERVENTION:
Magnesium (300 mg elemental Mg per day in two divided doses) or placebo was given orally for 12 months.

MAIN OUTCOME MEASURE:
The primary outcome measure was interval change in bone mineral content (BMC) of the total hip, femoral neck, Ward's area, and lumbar spine (L1-L4) after 12 months of Mg supplementation.

RESULTS:
Significantly increased accrual (P = 0.05) in integrated hip BMC occurred in the Mg-supplemented vs. placebo group. Trends for a positive Mg effect were evident in the pre- and early puberty and in mid-late puberty. Lumbar spinal BMC accrual was slightly (but not significantly) greater in the Mg-treated group. Compliance was excellent; 73% of capsules were ingested as inferred by pill counts. Serum mineral levels, calciotropic hormones, and bone markers were similar between groups.

CONCLUSIONS:
Oral Mg oxide capsules are safe and well tolerated. A positive effect of Mg supplementation on integrated hip BMC was evident in this small cohort.

Source
Carpenter TO, et al. A randomized controlled study of effects of dietary magnesium oxide supplementation on bone mineral content in healthy girls. J Clin Endocrinol Metab. 2006 Dec;91(12):4866-72.

Antenatal and Postnatal Iron Supplementation and Childhood Mortality in Rural Nepal: A Prospective Follow-up in a Randomized, controlled Community Trial

ABSTRACT
The long-term benefits of antenatal iron supplementation in child survival are not known. In 1999-2001, 4,926 pregnant women in rural Nepal participated in a cluster-randomized, double-masked, controlled trial involving 4 alternative combinations of micronutrient supplements, each containing vitamin A. The authors examined the impact on birth weight and early infant mortality in comparison with controls, who received vitamin A only. They followed the surviving offspring of these women at approximately age 7 years to study effects of in utero supplementation on survival. Of 4,130 livebirths, 209 infants died in the first 3 months and 8 were lost to follow-up. Of those remaining, 3,761 were followed, 150 died between ages 3 months and 7 years, and 152 were lost to follow-up. Mortality rates per 1,000 child-years from birth to age 7 years differed by maternal supplementation group, as follows: folic acid, 13.4; folic acid-iron, 10.3; folic acid-iron-zinc, 12.0; multiple micronutrients; 14.0; and controls, 15.2. Hazard ratios were 0.90 (95% confidence interval (CI): 0.65, 1.22), 0.69 (95% CI: 0.49, 0.99), 0.80 (95% CI: 0.58, 1.11), and 0.93 (95% CI: 0.66, 1.31), respectively, in the 4 supplementation groups. Maternal iron-folic acid supplementation reduced mortality among these children by 31% between birth and age 7 years. These results provide additional motivation for strengthening antenatal iron-folic acid programs.

Source
Christian P, et al. Antenatal and Postnatal Iron Supplementation and Childhood Mortality in Rural Nepal: A Prospective Follow-up in a Randomized, controlled Community Trial. am J of epid. 2009 Sep;170 (9): 1127-1136.

Omega-3 fatty acids and pregnancy

ABSTRACT
Omega-3 fatty acids are essential fatty acids that must be consumed in the diet.

Adequate consumption of omega-3 fatty acids is vitally important during pregnancy as they are critical building blocks of fetal brain and retina. Omega-3 fatty acids may also play a role in determining the length of gestation and in preventing perinatal depression. The most biologically active forms of omega-3 fatty acids are docosahexaenoic acid and eicosapentaenoic acid, which are primarily derived from marine sources such as seafood and algae. Recent surveys, however, indicate that pregnant women in the United States and in other countries eat little fish and therefore do not consume enough omega-3 fatty acids, primarily due to concern about the adverse effects of mercury and other contaminants on the developing fetus. This review discusses the benefits of omega-3 fatty acid consumption during pregnancy and provides guidelines for obstetricians advising patients.

Source
Coletta JM et al. Omega-3 fatty acids and pregnancy. Rev Obstet Gynecol 3:163-71, 2010.

Prenatal fatty acid status and child adiposity at age 3 y: results from a US pregnancy cohort

ABSTRACT

BACKGROUND:
Exposure to polyunsaturated fatty acids (PUFAs) in early life may influence adiposity development.

OBJECTIVE:
We examined the extent to which prenatal n-3 (omega-3) and n-6 (omega-6) PUFA concentrations were associated with childhood adiposity.

DESIGN:
In mother-child pairs in the Project Viva cohort, we assessed midpregnancy fatty acid intakes (n = 1120), maternal plasma PUFA concentrations (n = 227), and umbilical cord plasma PUFA concentrations (n = 302). We performed multivariable regression analyses to examine independent associations of n-3 PUFAs, including docosahexaenoic and eicosapentaenoic acids (DHA + EPA), n-6 PUFAs, and the ratio of n-6:n-3 PUFAs, with child adiposity at age 3 y measured by the sum of subscapular and triceps skinfold thicknesses (SS + TR) and risk of obesity (body mass index ≥95th percentile for age and sex).

RESULTS:
Mean (±SD) DHA + EPA intake was 0.15 ± 0.14 g DHA + EPA/d, maternal plasma concentration was 1.9 ± 0.6%, and umbilical plasma concentration was 4.6 ± 1.2%. In children, SS + TR was 16.7 ± 4.3 mm, and 9.4% of children were obese. In the adjusted analysis, there was an association between each SD increase in DHA + EPA and lower child SS + TR [-0.31 mm (95% CI: -0.58, -0.04 mm) for maternal diet and -0.91 mm (95% CI: -1.63, -0.20 mm) for cord plasma] and lower odds of obesity [odds ratio (95% CI): 0.68 (0.50, 0.92) for maternal diet and 0.09 (0.02, 0.52) for cord plasma]. Maternal plasma DHA + EPA concentration was not significantly associated with child adiposity. A higher ratio of cord plasma n-6:n-3 PUFAs was associated with higher SS + TR and odds of obesity.

CONCLUSION:
An enhanced maternal-fetal n-3 PUFA status was associated with lower childhood adiposity.

Source
Donahue SM, et al. Prenatal fatty acid status and child adiposity at age 3 y: results from a US pregnancy cohort. am J clin nutr. 2011 Feb 10. [Epub ahead of print]

Associations of maternal serum concentrations of antioxidants with Asthma in children; Proceedings of the Midwest Nursing Research Society

ABSTRACT

INTRODUCTION:
Studies linking maternal serum concentrations of carotenoids with asthma in children are lacking. The objective of this study was to examine the relationships of life-time doctor-diagnosed asthma in children with maternal serum levels of beta-carotene, alpha-carotene, and beta-cryptoxanthin in a population-based and representative sample of the United States' children.

METHODS:
This cross-sectional study analyzed data on 2290 pairs of mothers and their children aged 2 months-6 years who were examined in the third National Health and Nutrition Examination Survey (NHANES III). Bivariate and multiple logistic regression analyses were conducted treating serum concentrations of the antioxidants as categorical variables (quintiles). IRB approval was deemed unnecessary because the study was based on publicly available data.

RESULTS:
Mothers of children with asthma had significantly lower serum concentrations of alpha-carotene, beta-carotene, and beta-cryptoxanthin than mothers of children without asthma with significant does-dependent inverse associations between serum levels of these nutrients and the odds of asthma. The odds ratios (ORs) comparing children of mothers whose serum concentrations were in the 5th quintile with children whose mothers' serum concentrations were in the 1st quintile were 2.53 (95% CI: 1.06-6.03), 3.48 (95% CI: 1.32-9.17), and 2.60 (95% CI: 1.24-5.47), for alpha-carotene, beta-carotene, and beta-cryptoxanthin, respectively, with significant tests for trends obtained for the three nutrient markers. These associations persisted after adjusting for age, sex, ethnicity, maternal smoking during pregnancy, and educational level of the family reference person.

CONCLUSION:
Our study demonstrated inverse associations of maternal serum levels of alpha-carotene, beta-carotene, and beta-cryptoxanthin with the odds of asthma in children. These findings add to the growing body of literature linking asthma in children with maternal dietary factors and highlight the need for longitudinal studies to further examine the relationships of maternal diet during pregnancy or early in the child's life with the risk of asthma in children.

Source
Eldeirawi, K. Associations of maternal serum concentrations of antioxidants with Asthma in children; Proceedings of the Midwest Nursing Research Society. University of Illinois at Chicago: College of Nursing-Health Systems Science; 15 April 2010.

Dietary PUFA for preterm and term infants: review of clinical studies

ABSTRACT
Human milk contains n-3 and n-6 LCPUFA (long chain polyunsaturated fatty acids), which are absent from many infant formulas. During neonatal life, there is a rapid accretion of AA (arachidonic acid) and DHA (docosahexaenoic acid) in infant brain, DHA in retina and of AA in the whole body. The DHA status of breast-fed infants is higher than that of formula-fed infants when formulas do not contain LCPUFA. Studies report that visual acuity of breast-fed infants is better than that of formula-fed infants, but other studies do not find a difference. Cognitive development of breast-fed infants is generally better, but many sociocultural confounding factors may also contribute to these differences. The effect of dietary LCPUFA on FA status, immune function, visual, cognitive, and motor functions has been evaluated in preterm and term infants. Plasma and RBC FA status of infants fed formulas supplemented with both n-3 and n-6 LCPUFA was closer to the status of breast-fed infants than to that of infants fed formulas containing no LCPUFA. Adding n-3 LCPUFA to preterm-infant formulas led to initial beneficial effects on visual acuity. Few data are available on cognitive function, but it seems that in preterm infants, feeding n-3 LCPUFA improved visual attention and cognitive development compared with infants receiving no LCPUFA. Term infants need an exogenous supply of AA and DHA to achieve similar accretion of fatty acid in plasma and RBC (red blood cell) in comparison to breast-fed infants. Fewer than half of all studies have found beneficial effects of LCPUFA on visual, mental, or psychomotor functions. Improved developmental scores at 18 mo of age have been reported for infants fed both AA and DHA. Growth, body weight, and anthropometrics of preterm and term infants fed formulas providing both n-3 and n-6 LCPUFA fatty acids is similar in most studies to that of infants fed formulas containing no LCPUFA. A larger double-blind multicenter randomized study has recently demonstrated improved growth and developmental scores in a long-term feeding study of preterm infants. Collectively, the body of literature suggests that LCPUFA is important to the growth and development of infants. Thus, for preterm infants we recommend LCPUFA intakes in the range provided by feeding of human milk typical of mothers in Western countries. This range can be achieved by a combination of AA and DHA, providing an AA to DHA ratio of approximately 1.5 and a DHA content of as much as 0.4%. Preterm infants may benefit from slightly higher levels of these fatty acids than term infants. In long-term studies, feeding more than 0.2% DHA and 0.3% AA improved the status of these fatty acids for many weeks after DHA; AA was no longer present in the formula, enabling a DHA and AA status more similar to that of infants fed human milk. The addition of LCPUFA in infant formulas for term infants, with appropriate regard for quantitative and qualitative qualities, is safe and will enable the formula-fed infant to achieve the same blood LCPUFA status as that of the breast-fed infant.

Source
Fleith M, Clandinin MT. Dietary PUFA for preterm and term infants: review of clinical studies. Crit Rev Food Sci Nutr. 2005;45(3):205-29

Calcium and vitamin-D supplementation on bone structural properties in peripubertal female identical twins: a randomized controlled trial

ABSTRACT
A randomised controlled trial was used in assessing the impact of 6 months of daily calcium and vitamin-D supplementation on trabecular and cortical bone acquisition at distal tibial and radial sites using peripheral quantitative computed tomography (pQCT). Daily supplementation was associated with increased bone density and bone strength at the distal tibia and radius.

INTRODUCTION:
pQCT has not been used to assess bone responses to calcium and vitamin-D supplementation on peripubertal children. This randomised controlled trial aimed to assess the impact of a 6-month daily calcium and vitamin-D supplementation on trabecular and cortical bone acquisition at distal tibial and radial sites using pQCT.

METHODS:
Twenty pairs of peripubertal female identical twins, aged 9 to 13 years, were randomly assigned to receive either 800 mg of calcium and 400 IU of vitamin D3, or a matched placebo. Bone structural properties at the distal tibia and distal radius were acquired at baseline and 6 months.

RESULTS:
The calcium-supplemented group showed greater gains in trabecular density, trabecular area and strength strain index at the 4% of distal tibial and radial sites compared with the placebo group (p=0.001). Greater gains in cortical area at the 38% and 66% of tibial sites were also found in twins receiving the calcium supplement (p=0.001).

CONCLUSIONS:
Daily supplementation for a period of 6 months was associated with increased trabecular area, trabecular density and strength strain index at the ultra-distal tibia and radius and increased cortical area at tibial mid-shaft.

Source
Greene DA, et al. Calcium and vitamin-D supplementation on bone structural properties in peripubertal female identical twins: a randomized controlled trial. osteoporos Int. 2011 Feb;22(2):489-98. Epub 2010 Jun 11.

Mild iodine deficiency during pregnancy is associated with reduced educational outcomes in the offspring: 9-year follow-up of the gestational iodine cohort

ABSTRACT

CONTEXT:

Severe iodine deficiency (ID) during gestation is associated with neurocognitive sequelae. The long-term impact of mild ID, however, has not been well characterized.

OBJECTIVE:

The purpose of this study was to determine whether children born to mothers with urinary iodine concentrations (UICs) <150 µg/L during pregnancy have poorer educational outcomes in primary school than peers whose mothers did not have gestational ID (UIC ≥150 µg/L).

DESIGN:

This was a longitudinal follow-up (at 9 years old) of the Gestational Iodine Cohort. Pregnancy occurred during a period of mild ID in the population, with the children subsequently growing up in an iodine-replete environment.

SETTING AND PARTICIPANTS:

Participants were children whose mothers attended The Royal Hobart Hospital (Tasmania) antenatal clinics between 1999 and 2001.

MAIN OUTCOME MEASURES:

Australian national curriculum and Tasmanian state curriculum educational assessment data for children in year 3 were analyzed.

RESULTS:

Children whose mothers had UIC <150 µg/L had reductions of 10.0% in spelling (-41.1 points, 95% confidence interval [CI], -68.0 to -14.3, P = .003), 7.6% in grammar (-30.9 points, 95% CI, -60.2 to -1.7, P = .038), and 5.7% in English-literacy (-0.33 points, 95% CI, -0.63 to -0.03, P = .034) performance compared with children whose mothers' UICs were ≥150 µg/L. These associations remained significant after adjustment for a range of biological factors (maternal age at birth of child, gestational length at time of birth, gestational age at time of urinary iodine collection, birth weight, and sex). Differences in spelling remained significant after further adjustment for socioeconomic factors (maternal occupation and education).

CONCLUSIONS:

This study provides preliminary evidence that even mild iodine deficiency during pregnancy can have long-term adverse impacts on fetal neurocognition that are not ameliorated by iodine sufficiency during childhood.

Source

Hynes KL, Otahal P, Hay I, Burgess JR. Mild iodine deficiency during pregnancy is associated with reduced educational outcomes in the offspring: 9-year follow-up of the gestational iodine cohort. J Clin Endocrinol Metab. 2013;98(5):1954-62.

Prenatal docosahexaenoic acid supplementation and infant morbidity: randomized controlled trial

ABSTRACT

OBJECTIVE:

Long-chain polyunsaturated fatty acids such as docosahexaenoic acid (DHA) influence immune function and inflammation; however, the influence of maternal DHA supplementation on infant morbidity is unknown. We investigated the effects of prenatal DHA supplementation on infant morbidity.

METHODS:

In a double-blind randomized controlled trial conducted in Mexico, pregnant women received daily supplementation with 400 mg of DHA or placebo from 18 to 22 weeks' gestation through parturition. In infants aged 1, 3, and 6 months, caregivers reported the occurrence of common illness symptoms in the preceding 15 days.

RESULTS:

Data were available at 1, 3, and 6 months for 849, 834, and 834 infants, respectively. The occurrence of specific illness symptoms did not differ between groups; however, the occurrence of a combined measure of cold symptoms was lower in the DHA group at 1 month (OR: 0.76; 95% CI: 0.58–1.00). At 1 month, the DHA group experienced 26%, 15%, and 30% shorter duration of cough, phlegm, and wheezing, respectively, but 22% longer duration of rash (all P ≤ .01). At 3 months, infants in the DHA group spent 14% less time ill (P < .0001). At 6 months, infants in the DHA group experienced 20%, 13%, 54%, 23%, and 25% shorter duration of fever, nasal secretion, difficulty breathing, rash, and "other illness," respectively, but 74% longer duration of vomiting (all P < .05).

CONCLUSIONS:

DHA supplementation during pregnancy decreased the occurrence of colds in children at 1 month and influenced illness symptom duration at 1, 3, and 6 months.

Source

Imhoff-Kunsch B, Stein AD, Martorell R et al. Prenatal docosahexaenoic acid supplementation and infant morbidity: randomized controlled trial. Pediatrics.2011; 128(3):505-12.

Long-term effects of prenatal omega-3 fatty acid intake on visual function in school-age children

ABSTRACT

OBJECTIVE:

To assess the long-term effect on visual development of omega-3 polyunsaturated fatty acid (n-3 PUFA) intake during gestation.

STUDY **DESIGN:**

Using visual evoked potentials (VEPs), the long-term effects on visual development were evaluated in 136 school-age Inuit children exposed to high levels of n-3 PUFAs during gestation. VEP protocols using color and motion stimuli were used to assess parvocellular and magnocellular responses. Concentrations of the two major n-3 PUFAs (docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) were measured in umbilical

cord and child plasma phospholipids, reflecting prenatal and postnatal exposure, respectively.

RESULTS:
After adjustment for confounders, cord plasma DHA level was found to be associated with shorter latencies of the N1 and P1 components of the color VEPs. No effects were found for current n-3 PUFA body burden or motion-onset VEPs.

CONCLUSION:
This study demonstrates beneficial effects of DHA intake during gestation on visual system function at school age. DHA is particularly important for the early development and long-term function of the visual parvocellular pathway.

Source
Jacques C, et al. Long-term effects of prenatal omega-3 fatty acid intake on visual function in school-age children. J Pediatr. 2011 Jan;158(1):83-90, 90.e1. Epub 2010 Aug 25.

Folate and neural tube defects

ABSTRACT
A protective effect of folate against the development of neural tube defects (NTDs), specifically, anencephaly and spina bifida, is now well recognized, having been established by a chain of clinical research studies over the past half century. This article summarizes the more important of these studies, which have led to the current situation in which all women capable of becoming pregnant are urged to ingest folic acid regularly. The recommended intakes are 4 mg/d for those at high risk (by virtue of a previous NTD pregnancy outcome) and 0.4 mg/d for all others. However, a reduction in NTD births did not follow promulgation of these recommendations, and so folic acid fortification was mandated in the United States and some other countries. Although some controversy remains about the adequacy of fortification levels, the process was followed by significant improvement in folate indexes and a reduction of 25-30% in NTD frequency (about one-half of the proportion of cases assumed to be responsive to folate). The folate-NTD relation represents the only instance in which a congenital malformation can be prevented simply and consistently. Nevertheless, several research gaps remain: identification of the mechanism by which the defect occurs and how folate ameliorates it; characterization of the relative efficacy of food folate, folic acid added to foods, and folic acid by itself; delineation of the dose-response relations of folate and NTD prevention; and more precise quantification of the dose needed to prevent recurrences.

Source
Pitkin RM. Folate and neural tube defects. Am J Clin Nutr 2007; 85(1): 285S-288S.

Lower maternal folate status in early pregnancy is associated with childhood hyperactivity and peer problems in offspring

ABSTRACT
BACKGROUND:
Maternal nutrition during pregnancy has been linked with fetal brain development and psychopathology in the offspring. We examined for associations of maternal folate status and dietary intake during pregnancy with brain growth and childhood behavioural difficulties in the offspring.

METHODS:

In a prospective cohort study, maternal red blood cell folate (RCF) was measured at 14 weeks of pregnancy and total folate intake (TFI) from food and supplements was assessed in early and late pregnancy. The offspring's head circumference and body weight were measured at birth and in infancy, and 100 mothers reported on children's behavioural difficulties at a mean age of 8.75 years using the Strengths and Difficulties Questionnaire.

RESULTS:
Lower maternal RCF and TFI in early pregnancy were associated with higher childhood hyperactivity (RCF: beta = -.24; p = .013; TFI: beta = -.24; p = .022) and peer problems scores (RCF: beta = -.28; p = .004; TFI: beta = -.28; p = .009) in the offspring. Maternal gestational RCF was positively associated with head circumference at birth (adjusted for gestational age), and mediation analyses showed significant inverse indirect associations of RCF with hyperactivity/inattention and peer problems via fetal brain growth. Adjustment for mother's smoking and drinking alcohol during pregnancy did not change the results.

CONCLUSIONS:
Although the associations are small and residual confounding is possible, our data provide preliminary support for the hypothesis that lower folate status in early pregnancy might impair fetal brain development and affect hyperactivity/inattention and peer problems in childhood.

Source
Schlotz W, et al. Lower maternal folate status in early pregnancy is associated with childhood hyperactivity and peer problems in offspring. J Child Psychol Psychiatry. 2010 May;51(5):594-602.

Periconception dietary intake of choline and betaine and neural tube defects in offspring

ABSTRACT
Periconceptional intake of folic acid prevents some neural tube defects (NTDs). Other nutrients may also contribute to NTD etiologies; a likely candidate is choline. Similar to folic acid, choline is involved in one-carbon metabolism for methylation of homocysteine to methionine. The authors investigated whether maternal periconceptional dietary intakes of choline and its metabolite betaine influence NTD risk. Data were derived from a case-control study of fetuses and infants with NTDs among 1989-1991 California births. In-person interviews were conducted with mothers of 424 NTD cases and with mothers of 440 nonmalformed controls. A standard 100-item food frequency questionnaire was used to assess nutrient intake. Dietary intakes of choline were associated with reduced NTD risks. Controlling for

intake of supplemental folic acid, dietary folate, dietary methionine, and other covariates did not substantially influence risk estimates for choline. NTD risk estimates were lowest for women whose diets were rich in choline, betaine, and methionine. That is, for women whose intake was above the 75th percentile compared with below the 25th percentile for all three nutrients, the odds ratio was 0.17 (95% confidence interval: 0.04, 0.76). Study findings for dietary components other than folic acid offer additional clues about the complex etiologies of NTDs.

Source
Shaw G et al. Periconception dietary intake of choline and betaine and neural tube defects in offspring. Am J Epidemiol 2004;160-102-109.

Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren

ABSTRACT

BACKGROUND:
To our knowledge, no rigorously designed clinical trials have evaluated the relation between vitamin D and physician-diagnosed seasonal influenza.

OBJECTIVE:
We investigated the effect of vitamin D supplements on the incidence of seasonal influenza A in schoolchildren.

DESIGN:
From December 2008 through March 2009, we conducted a randomized, double-blind, placebo-controlled trial comparing vitamin D(3) supplements (1200 IU/d) with placebo in schoolchildren. The primary outcome was the incidence of influenza A, diagnosed with influenza antigen testing with a nasopharyngeal swab specimen.

RESULTS:
Influenza A occurred in 18 of 167 (10.8%) children in the vitamin D(3) group compared with 31 of 167 (18.6%) children in the placebo group [relative risk (RR), 0.58; 95% CI: 0.34, 0.99; P = 0.04]. The reduction in influenza A was more prominent in children who had not been taking other vitamin D supplements (RR: 0.36; 95% CI: 0.17, 0.79; P = 0.006) and who started nursery school after age 3 y (RR: 0.36; 95% CI: 0.17, 0.78; P = 0.005). In children with a previous diagnosis of asthma, asthma attacks as a secondary outcome occurred in 2 children receiving vitamin D(3) compared with 12 children receiving placebo (RR: 0.17; 95% CI: 0.04, 0.73; P = 0.006).

CONCLUSION:
This study suggests that vitamin D(3) supplementation during the winter may reduce the incidence of influenza A, especially in specific subgroups of schoolchildren. This trial was registered at https://center.umin.ac.jp as UMIN000001373.

Source
Urashima M, et al. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr. 2010 May;91(5):1255-60.

Folic Acid Supplementation for the Prevention of Neural Tube Defects: An Update of the Evidence for the U.S. Preventive Services Task Force Rockville (MD): Agency for Healthcare Research and Quality (US)

ABSTRACT

BACKGROUND:
Neural tube defects (NTDs) are among the most common birth defects in the United States.

PURPOSE:
To update the evidence on folic acid supplementation in women of childbearing age for the prevention of neural tube defects in their offspring.

DATA SOURCES:
MEDLINE and Cochrane Library searches (from January 1995 through November 2007), recent systematic reviews, reference lists of retrieved articles, and expert suggestions.

STUDY SELECTION:
English language studies were selected to answer the following two questions: Does folic acid supplementation in women of childbearing age reduce the risk of a pregnancy affected by a neural tube defect? Does folic acid supplementation in women of childbearing age increase the risk of any harmful outcomes for either the woman or the infant? The following study types were selected: for potential benefits of folic acid—randomized, controlled trials (RCTs), case-control studies, cohort studies, systematic reviews and meta-analyses; for potential harms of folic acid—RCTs, case-control studies, systematic reviews, meta-analyses, and large observational studies.

DATA EXTRACTION:
All studies were reviewed, abstracted, and rated for quality using predefined U.S. Preventive Services Task Force criteria.

Data Synthesis:

Four observational studies reported benefit, in reduction of risk of NTD associated with folic acid-containing supplements. Differences in study type and methods prevent the calculation of a summary of the reduction in risk. The one included study on harms reported that the association of twinning with folic acid intake disappeared after adjusting for in vitro fertilization and for underreporting of folic acid intake.

Limitations:

There is limited evidence on dose. We found no evidence on the potential harm of masking vitamin B12 deficiency in women of childbearing age. Our search focused on NTDs and therefore does not provide a comprehensive review of the effects of folic acid on all possible outcomes.

CONCLUSIONS:

New observational evidence supports previous RCT evidence that folic acid—containing supplements reduce the risk of NTD-affected pregnancies. The association of folic acid use with twin gestation may be confounded by fertility interventions including ovulation simulation and in vitro fertilization.

Source
Wolff T, Witkop CT, Miller T, Syed SB. Folic Acid Supplementation for the Prevention of Neural Tube Defects: An Update of the Evidence for the U.S. Preventive Services Task Force Rockville (MD): Agency for Healthcare Research and Quality (US); 2009 May. R

COGNITIVE HEALTH

Antioxidative and anti-inflammatory neuroprotective effects of astaxanthin and canthaxanthin in nerve growth factor differentiated PC12 cells

ABSTRACT
Nerve growth factor differentiated PC12 cells were used to examine the antioxidative and anti-inflammatory effects of astaxanthin (AX) and canthaxanthin (CX). PC12 cells were pretreated with AX or CX at 10 or 20 muM, and followed by exposure of hydrogen peroxide (H(2)O(2)) or 1-methyl-4-phenylpyridinium ion (MPP(+)) to induce cell injury. H(2)O(2) or MPP(+) treatment significantly decreased cell viability, increased lactate dehydrogenase (LDH) release, enhanced DNA fragmentation, and lowered mitochondrial membrane potential (MMP) ($P < 0.05$). The pretreatments from AX or CX concentration-dependently alleviated H(2)O(2) or MPP(+)-induced cell death, LDH release, DNA fragmentation, and MMP reduction ($P < 0.05$). Either H(2)O(2) or MPP(+) treatment significantly increased malonyldialdehyde (MDA) and reactive oxygen species (ROS) formations, decreased glutathione content, and lowered glutathione peroxidase (GPX) and catalase activities ($P < 0.05$). The pretreatments from AX or CX significantly retained GPX and catalase activities, and decreased MDA and ROS formations ($P < 0.05$). H(2)O(2) or MPP(+) treatment significantly decreased Na(+)-K(+)-ATPase activity, elevated caspase-3 activity and levels of interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-alpha ($P < 0.05$); and the pretreatments from these agents significantly restored Na(+)-K(+)-ATPase activity, suppressed caspase-3 activity and release of IL-1, IL-6, and TNF-alpha ($P < 0.05$). Based on the observed antioxidative and anti-inflammatory protection from AX and CX, these 2 compounds were potent agents against neurodegenerative disorder.

Source
Chan KC, et al. Antioxidative and anti-inflammatory neuroprotective effects of astaxanthin and canthaxanthin in nerve growth factor differentiated PC12 cells. J Food Sci. 2009 Sep;74(7):H225-31.

Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: a randomized controlled trial

ABSTRACT
BACKGROUND:
Homocysteine is a risk factor for Alzheimer's disease. In the first report on the VITACOG trial, we showed that homocysteine-lowering treatment with B vitamins slows the rate of brain atrophy in mild cognitive impairment (MCI). Here we report the effect of B vitamins oncognitive and clinical decline (secondary outcomes) in the same study.

METHODS:

This was a double-blind, single-centre study, which included participants with MCI, aged ≥ 70 y, randomly assigned to receive a daily dose of 0.8 mg folic acid, 0.5 mg vitamin B(12) and 20 mg vitamin B(6) (133 participants) or placebo (133 participants) for 2 y. Changes in cognitiveor clinical function were analysed by generalized linear models or mixed-effects models.

RESULTS:
The mean plasma total homocysteine was 30% lower in those treated with B vitamins relative to placebo. B vitamins stabilized executive function (CLOX) relative to placebo ($P = 0.015$). There was significant benefit of B-vitamin treatment among participants with baseline homocysteine above the median (11.3 μmol/L) in global cognition (Mini Mental State Examination, $P < 0.001$), episodic memory (Hopkins Verbal Learning Test-delayed recall, $P = 0.001$) and semantic memory (category fluency, $P = 0.037$). Clinical benefit occurred in the B-vitamin group for those in the upper quartile of homocysteine at baseline in global clinical dementia rating score ($P = 0.02$) and IQCODE score ($P = 0.01$).

CONCLUSION:
In this small intervention trial, B vitamins appear to slow cognitive and clinical decline in people with MCI, in particular in those with elevated homocysteine. Further trials are needed to see if this treatment will slow or prevent conversion from MCI to dementia.

Source
de Jager CA et al. Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: a randomized controlled trial. Int J Geriatr Psychiatry [Epub ahead of print, July, 2011]

Dietary choline and betaine intakes in relationship to concentrations of inflammatory markers in healthy adults: the ATTICA study

ABSTRACT
BACKGROUND:
Choline and betaine are found in a variety of plant and animal foods and were recently shown to be associated with decreased homocysteine concentrations.

OBJECTIVE:
The scope of this work was to investigate the associations between dietary choline and betaine consumption and various markers of low-grade systemic inflammation.

DESIGN:
Under the context of a cross-sectional survey that enrolled 1514 men (18-87 y of age) and 1528 women (18-89 y of age) with no

history of cardiovascular disease (the ATTICA Study), fasting blood samples were collected and inflammatory markers were measured. Dietary habits were evaluated with a validated food-frequency questionnaire, and the intakes of choline and betaine were calculated from food-composition tables.

RESULTS:
Compared with the lowest tertile of choline intake (<250 mg/d), participants who consumed >310 mg/d had, on average, 22% lower concentrations of C-reactive protein ($P < 0.05$), 26% lower concentrations of interleukin-6 ($P < 0.05$), and 6% lower concentrations of tumor necrosis factor-alpha ($P < 0.01$). Similarly, participants who consumed >360 mg/d of betaine had, on average, 10% lower concentrations of homocysteine ($P < 0.01$), 19% lower concentrations of C-reactive protein ($P < 0.1$), and 12% lower concentrations of tumor necrosis factor-alpha ($P < 0.05$) than did those who consumed <260 mg/d. These findings were independent of various sociodemographic, lifestyle, and clinical characteristics of the participants.

CONCLUSIONS:
Our results support an association between choline and betaine intakes and the inflammation process in free-eating and apparently healthy adults. However, further studies are needed to confirm or refute our findings.

Source
Detopoulou P et al. Dietary choline and betaine intakes in relationship to concentrations of inflammatory markers in healthy adults: the ATTICA study. Am J Clin Nutr 2008;87:424-430.

Physicians and nurses use and recommend dietary supplements: report of a survey

ABSTRACT
BACKGROUND:
Numerous surveys show that dietary supplements are used by a large proportion of the general public, but there have been relatively few surveys on the prevalence of dietary supplement use among health professionals, including physicians and nurses. Even less information is available regarding the extent to which physicians and nurses recommend dietary supplements to their patients.

METHODS:
An online survey was administered in October 2007 to 900 physicians and 277 nurses by Ipsos Public Affairs for the Council for Responsible Nutrition (CRN), a trade association representing the dietary supplement industry. The health professionals were asked whether they used dietary supplements and their reasons for doing so, and whether they recommend dietary supplements to their patients.

RESULTS:
The "Life...supplemented" Healthcare Professionals Impact Study (HCP Impact Study) found that 72% of physicians and 89% of nurses in this sample used dietary supplements regularly, occasionally, or seasonally. Regular use of dietary supplements was reported by 51% of physicians and 59% of nurses. The most common reason given for using dietary supplements was for overall health and wellness (40% of physicians and 48% of nurses), but more than two-thirds cited more than one reason for using the products. When asked whether they "ever recommend dietary supplements" to their patients, 79% of physicians and 82% of nurses said they did.

CONCLUSION:
Physicians and nurses are as likely as members of the general public to use dietary supplements, as shown by comparing the results of this survey with data from national health and nutrition surveys. Also, most physicians and nurses recommend supplements to their patients, whether or not the clinicians use dietary supplements themselves.

Source
Dickinson A, et al. Physicians and nurses use and recommend dietary supplements: report of a survey. Nutr J. 2009 Jul 1;8:29.

Preventing Alzheimer's disease-related gray matter atrophy by B-vitamin treatment

ABSTRACT
Is it possible to prevent atrophy of key brain regions related to cognitive decline and Alzheimer's disease (AD)? One approach is to modify nongenetic risk factors, for instance by lowering elevated plasma homocysteine using B vitamins. In an initial, randomized controlled study on elderly subjects with increased dementia risk (mild cognitive impairment according to 2004 Petersen criteria), we showed that high-dose B-vitamin treatment (folic acid 0.8 mg, vitamin B6 20 mg, vitamin B12 0.5 mg) slowed shrinkage of the whole brain volume over 2 y. Here, we go further by demonstrating that B-vitamin treatment reduces, by as much as seven fold, the cerebral atrophy in those gray matter (GM) regions specifically vulnerable to the AD process, including the medial temporal lobe. In the placebo group, higher homocysteine levels at baseline are associated with faster GM atrophy, but this deleterious effect is largely prevented by B-vitamin treatment. We additionally show that the beneficial effect of B vitamins is confined to participants with high homocysteine (above the median, 11 μmol/L) and that, in these participants, a causal Bayesian network analysis indicates the following chain of events: B vitamins lower homocysteine, which directly leads to a decrease in GM atrophy, thereby slowing cognitive decline. Our results show that B-vitamin supplementation can slow the atrophy of specific brain regions that are a key component of the AD process and that are associated with cognitive decline. Further B-vitamin supplementation trials focusing on elderly subjets with high homocysteine levels are warranted to see if progression to dementia can be prevented.

Source
Douaud G. et. al. Preventing Alzheimer's disease-related gray matter atrophy by B-vitamin treatment. PNAS 2013:119(23):9523-9528.

Effects of dietary supplements on depressive symptoms in older patients: A randomized double-blind placebo-controlled trial

ABSTRACT

BACKGROUND:

High total plasma homocysteine (tHcy) levels may cause neurotransmitter deficiency, and consequently depression of mood. We have recently shown that mixed oral nutritional supplements containing B-group vitamins led to a statistically significant benefit on depressive symptoms. The aim of this report was to examine the association between elevated plasma tHcy and symptoms of depression in older patients.

METHODS:

Two-hundred and thirty-six hospitalised acutely ill older patients, who were part of a randomised double-blind placebo-controlled trial, were assigned to receive daily mixed oral nutritional supplements containing B-group vitamins or a placebo for 6 weeks. Outcome measures included symptoms of depression measured using Geriatric Depression score and plasma tHcy levels.

RESULTS:

The mean tHcy concentration fell by 22% among patients given the supplements compared with the placebo group (mean difference 4.1 µmol/l (95% CI: 0.14–8.03), P = 0.043). tHcy concentrations was divided into four quartiles and analysed against depression scores. tHcy concentrations in the first relative to the fourth quartile of the distribution were associated with a lower depression symptoms at the end of the supplement period (Geriatric depression score r = –0.20, P=0.042).

CONCLUSIONS:

Lower plasma tHcy concentrations were associated with reduced depression symptoms in older patients recovering from acute illness.

Source

Gariballa S and Forster S. Effects of dietary supplements on depressive symptoms in older patients: A randomized double-blind placebo-controlled trial. Clinical Nutrition 26:545-51, 2007.

Docosapentaenoic acid (22:5n-3): a review of its biological effects.

ABSTRACT

This article summarizes the current knowledge available on metabolism and the biological effects of n-3 docosapentaenoic acid (DPA). n-3 DPA has not been extensively studied because of the limited availability of the pure compound. n-3 DPA is an elongated metabolite of EPA and is an intermediary product between EPA and DHA. The literature on n-3 DPA is limited, however the available data suggests it has beneficial health effects. In vitro n-3 DPA is retro-converted back to EPA, however it does not appear to be readily metabolised to DHA. In vivo studies have shown limited conversion of n-3 DPA to DHA, mainly in liver, but in addition retro-conversion to EPA is evident in a number of tissues. n-3 DPA can be metabolised by lipoxygenase, in platelets, to form ll-hydroxy-7,9,13,16,19- and 14-hydroxy-7,10,12,16,19-DPA. It has also been reported that n-3 DPA is effective (more so than EPA and DHA) in inhibition of aggregation in platelets obtained from rabbit blood. In addition, there is evidence that n-3 DPA possesses 10-fold greater endothelial cell migration ability than EPA, which is important in wound-healing processes. An in vivo study has reported that n-3 DPA reduces the fatty acid synthase and malic enzyme activity levels in n-3 DPA-supplemented mice and these effects were stronger than the EPA-supplemented mice. Another recent in vivo study has reported that n-3 DPA may have a role in attenuating age-related decrease in spatial learning and long-term potentiation. However, more research remains to be done to further investigate the biological effects of this n-3 VLCPUFA.

Source

Kaur G, et al. Docosapentaenoic acid (22:5n-3): a review of its biological effects. Progressive Lipid Research. 2011 Jan; 50(1):28-34

Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males

ABSTRACT

RATIONALE

A significant proportion of the general population report supplementing their diet with one or more vitamins or minerals, with common reasons for doing so being to combat stress and fatigue and to improve mental functioning. Few studies have assessed the relationship between supplementation with vitamins/minerals and psychological functioning in healthy cohorts of non-elderly adults.

OBJECTIVES:

The present randomised, placebo-controlled, double–blind, parallel groups trial assessed the cognitive and mood effects of a high-dose B-complex vitamin and mineral supplement (Berocca®) in 215 males aged 30 to 55 years, who were in full-time employment.

METHODS:

Participants attended the laboratory prior to and on the last day of a 33-day treatment period where they completed the Profile of Mood States (POMS), Perceived Stress Scale (PSS) and General Health Questionnaire (GHQ-12). Cognitive performance and task-related modulation of mood/fatigue were assessed with the 60 min cognitive demand battery. On the final day, participants also completed the Stroop task for 40 min whilst engaged in inclined treadmill walking and subsequent executive function was assessed.

RESULTS:

Vitamin/mineral supplementation led to significant improvements in ratings on the PSS, GHQ-12 and the 'vigour' subscale of the POMS. The vitamin/mineral group also performed better on the Serial 3s subtractions task and rated themselves as less 'mentally tired' both pre- and post-completion of the

cognitive demand battery.

CONCLUSIONS:
Healthy members of the general population may benefit from augmented levels of vitamins/minerals via direct dietary supplementation. Specifically, supplementation led to improved ratings of stress, mental health and vigour and improved cognitive performance during intense mental processing.

Source
Kennedy DO et al. Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. Psychopharmacol 211:55-68, 2010.

Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial

ABSTRACT
Observational studies have linked lower omega-3 (n-3) polyunsaturated fatty acids (PUFAs) and higher omega-6 (n-6) PUFAs with inflammation and depression, but randomized controlled trial (RCT) data have been mixed. To determine whether n-3 decreases proinflammatory cytokine production and depressive and anxiety symptoms in healthy young adults, this parallel group, placebo-controlled, double-blind 12-week RCT compared n-3 supplementation with placebo. The participants, 68 medical students, provided serial blood samples during lower-stress periods as well as on days before an exam. The students received either n-3 (2.5 g/d, 2085 mg eicosapentaenoic acid and 348 mg docosahexanoic acid) or placebo capsules that mirrored the proportions of fatty acids in the typical American diet. Compared to controls, those students who received n-3 showed a 14% decrease in lipopolysaccharide (LPS) stimulated interleukin 6 (IL-6) production and a 20% reduction in anxiety symptoms, without significant change in depressive symptoms. Individuals differ in absorption and metabolism of n-3 PUFA supplements, as well as in adherence; accordingly, planned secondary analyses that used the plasma n-6:n-3 ratio in place of treatment group showed that decreasing n-6:n-3 ratios led to lower anxiety and reductions in stimulated IL-6 and tumor necrosis factor alpha (TNF-α) production, as well as marginal differences in serum TNF-α. These data suggest that n-3 supplementation can reduce inflammation and anxiety even among healthy young adults. The reduction in anxiety symptoms associated with n-3 supplementation provides the first evidence that n-3 may have potential anxiolytic benefits for individuals without an anxiety disorder diagnosis.

Source
Kiecolt-Glaser JK et al. Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial. Brain Behav Immun 25:1725-34, 2011.

Serum 25-Hydroxyvitamin D Concentration and Cognitive Impairment

ABSTRACT
Vitamin D may be of interest in the prevention of cognitive impairment, though previous findings are inconclusive. Participants were 1766 adults aged 65 years and older from the Health Survey for England 2000, a nationally representative population-based study. Cognitive impairment was assessed using the Abbreviated Mental Test Score. The cross-sectional relation of serum 25-hydroxyvitamin D quartiles to cognitive impairment was modeled using logistic regression. In all, 212 participants (12%) were cognitively impaired. Odds ratios (95% confidence intervals) for cognitive impairment in the first (8-30 nmol/L), second (31-44 nmol/L), and third (45-65 nmol/L) quartiles of serum 25-hydroxyvitamin D compared with the fourth (66-170 nmol/L) were 2.3 (1.4-3.8), 1.4 (0.8-2.4), and 1.1 (0.6-1.9), after adjustment for age, sex, education, ethnicity, season of testing, and additional risk factors for cognitive impairment (P for linear trend = .001). Our data suggest low serum 25-hydroxyvitamin D is associated with increased odds ofcognitive impairment.

Source
Llewellyn DJ, et al. Serum 25-Hydroxyvitamin D Concentration and Cognitive Impairment. J Geriatr Psychiatry Neurol. 2009 Feb; 22 (3): 188–95.

Serum phospholipid docosahexaenoic acid is associated with cognitive functioning during middle adulthood

ABSTRACT
Existing evidence links greater dietary intake of fish and (n-3) PUFA to better early brain development and lowered risk of cognitive disorders in late life. The mechanisms for these associations remain unclear and may be related to specific (n-3) fatty acids and may concern cognitive function generally rather than only early brain development and age-related cognitive dysfunction. In this investigation, we tested potential associations between (n-3) fatty acids in serum phospholipids and major dimensions of cognitive functioning in mid-life adults. Participants were 280 community volunteers between 35 and 54 y of age, free of major neuropsychiatric disorders, and not taking fish oil supplements. Dietary biomarkers were alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenonic acid (DHA) in serum phospholipids measured using GC. Five major dimensions of cognitive functioning were assessed with a 75-min battery of neuropsychological tests. In covariate adjusted regression models, higher DHA (mol %) was related to better performance on tests of nonverbal reasoning and mental flexibility, working memory, and vocabulary (P <or= 0.05). These associations were generally linear. Associations between DHA and nonverbal reasoning and working memory persisted with additional adjustment for participant education and vocabulary scores (P <or= 0.05). Neither EPA nor ALA was nota-

bly related to any of the 5 tested dimensions of cognitive performance. Among the 3 key (n-3) PUFA, only DHA is associated with major aspects of cognitive performance in nonpatient adults <55 y old. These findings suggest that DHA is related to brain health throughout the lifespan and may have implications for clinicaltrials of neuropsychiatric disorders.

Source
Muldoon MF, et al. Serum phospholipid docosahexaenoic acid is associated with cognitive functioning during middle adulthood. J Nutr. 2010 Apr;140(4):848-53.

Obesity phenotypes in midlife and cognition in early old age

ABSTRACT

OBJECTIVE:

To examine the association of body mass index (BMI) and metabolic status with cognitive function and decline.

METHODS:

A total of 6,401 adults (71.2% men), aged 39–63 years in 1991–1993, provided data on BMI (normal weight 18.5–24.9 kg/m2, overweight 25–29.9 kg/m2; and obese ≥30 kg/m2) and metabolic status (abnormality defined as 2 or more of 1) triglycerides ≥1.69 mmol/L or lipid-lowering drugs, 2) systolic blood pressure ≥130 mm Hg, diastolic blood pressure ≥85 mm Hg, or antihypertensive drugs, 3) glucose ≥5.6 mmol/L or medications for diabetes, and 4) high-density lipoprotein cholesterol <1.04 mmol/L for men and <1.29 mmol/L for women). Four cognitive tests (memory, reasoning, semantic, and phonemic fluency) were administered in 1997–1999, 2002–2004, and 2007–2009, standardized to z scores, and averaged to yield a global score.

RESULTS:

Of the participants, 31.0% had metabolic abnormalities, 52.7% were normal weight, 38.2% were overweight, and 9.1% were obese. Among the obese, the global cognitive score at baseline (p = 0.82) and decline (p = 0.19) over 10 years was similar in the metabolically normal and abnormal groups. In the metabolically normal group, the 10-year decline in the global cognitive score was similar (p for trend = 0.36) in the normal weight (–0.40; 95% confidence interval [CI] –0.42 to –0.38), overweight (–0.42; 95% CI –0.45 to –0.39), and obese (–0.42; 95% CI –0.50 to –0.34) groups. However, in the metabolically abnormal group, the decline on the global score was faster among obese (–0.49; 95% CI –0.55 to –0.42) than among normal weight individuals (–0.42; 95% CI –0.50 to –0.34), (p = 0.03).

CONCLUSIONS:

In these analyses the fastest cognitive decline was observed in those with both obesity and metabolic abnormality.

Prospective studies suggest that overweight and obesity, particularly in midlife, are risk factors for dementia. Early studies relating adiposity to dementia provided conflicting results until it became evident that age modified this association. Higher body mass index (BMI) in elderly individuals is associated with lower dementia risk; possible explanations include weight loss during the preclinical phase of dementia (reverse causation) and selection biases because of competing risks of death related to high BMI. Recent evidence suggests that in younger populations, in whom dementia is rare, obesity is a risk factor for poor cognitive outcomes in cross-sectional and prospective analyses. It is hypothesized that obesity-related pathology that leads to cognitive decline takes many years to develop, and BMI in midlife rather than at older ages may reflect the long-term effect of obesity on cognition.

Although obesity is typically accompanied by unfavorable metabolic profiles, such as high glucose, adverse lipid levels, and elevated blood pressure, this is not always the case. Recent attempts to capture this heterogeneity include concepts such as metabolically healthy obesity (MHO), used to describe individuals with a BMI ≥30 kg/m^2 combined with an otherwise healthy metabolic profile. Although there is considerable evidence to show adverse effects of obesity on health, research suggests that the MHO phenotype is not associated with increased risk of cardiovascular disease. However, the evidence is far from conclusive, and little is known about the impact of MHO on cognitive function.

The objective of the present study was to examine the association between midlife obesity phenotypes, including MHO, and cognitive function in early old age. We also assess associations with cognitive decline, based on 3 assessments over 10 years. A standardized definition was used to categorize individuals based on their BMI and metabolic profile using data on dyslipidemia, hypertension, and hyperglycemia.

Source
Singh-Manoux A. et.al. Obesity phenotypes in midlife and cognition in early old age. The Whitehall II cohort study. Neurology 2012;79 (8):755-762.

Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in milk cognitive impairment: A randomized controlled trial

ABSTRACT

BACKGROUND:

An increased rate of brain atrophy is often observed in older subjects, in particular those who suffer from cognitive decline. Homocysteine is a risk factor for brain atrophy, cognitive impairment and dementia. Plasma concentrations of homocysteine can be lowered by dietary administration of B vitamins.

OBJECTIVE:

To determine whether supplementation with B vitamins that lower levels of plasma total homocysteine can slow the rate of brain atrophy in subjects with mild cognitive impairment in a randomised controlled trial (VITACOG, ISRCTN 94410159).

METHODS AND FINDINGS:

Single-center, randomized, double-blind controlled trial of high-dose folic acid,

vitamins B(6) and B(12) in 271 individuals (of 646 screened) over 70 y old with mild cognitive impairment. A subset (187) volunteered to have cranial MRI scans at the start and finish of the study. Participants were randomly assigned to two groups of equal size, one treated with folic acid (0.8 mg/d), vitamin B(12) (0.5 mg/d) and vitamin B(6) (20 mg/d), the other with placebo; treatment was for 24 months. The main outcome measure was the change in the rate of atrophy of the whole brain assessed by serial volumetric MRI scans.

RESULTS:
A total of 168 participants (85 in active treatment group; 83 receiving placebo) completed the MRI section of the trial. The mean rate of brain atrophy per year was 0.76% [95% CI, 0.63-0.90] in the active treatment group and 1.08% [0.94-1.22] in the placebo group (P = 0.001). Thetreatment response was related to baseline homocysteine levels: the rate of atrophy in participants with homocysteine >13 µmol/L was 53% lower in the active treatment group (P = 0.001). A greater rate of atrophy was associated with a lower final cognitive test scores. There was no difference in serious adverse events according to treatment category.

CONCLUSIONS AND SIGNIFICANCE:
The accelerated rate of brain atro phy in elderly with mild cognitive impairment can be slowed by treatmentwith homocysteine-lowering B vitamins. Sixteen percent of those over 70 y old have mild cognitive impairment and half of these develop Alzheimer's disease. Since accelerated brain atrophy is a characteristic of subjects with mild cognitive impairment who convert to Alzheimer's disease, trials are needed to see if the same treatment will delay the development of Alzheimer's disease.

Source
Smith AD, et al. Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in milk cognitive impairment: A randomized controlled trial. 2010:PloS ONE 5(9):e12244.

The effect of low-dose omega 3 fatty acids on the treatment of mild to moderate depression in the elderly: a double-blind, randomized, placebo-controlled study

ABSTRACT
Due to the rise in the social and economic costs of depression, new antidepressant medication with fewer side effects should be found. Several studies have shown that an association exists between ω-3 polyunsaturated fatty acids (ω-3 PUFAs) and depression. However, this association has not been clear enough in the elderly with mild to moderate depression. Sixty-six inhabitants of Kahrizak Charity Foundation participated in this double-blind, randomized, placebo-controlled study. Each participant was ≥ 65 years of age, had a Mini Mental State Exam of ≥ 22, and had scores ranging from 5 to 11 on the Geriatric Depression Scale-15 (GDS-15). During the 6 months, the drug group was treated daily with one gram of fish oil capsule containing 300 mg of both eicosapentaenoic acid and docosahexaenoic acid. No significant differences were noted between the groups in regard to level of education, use of antidepressant drugs, alcohol, tobacco use, history of chronic diseases, age, body mass index (BMI), high-sensitive C-reactive protein (hs-CRP), total cholesterol, and GDS-15 scores at baseline. After adjusting for cholesterol, BMI, and history of thyroid dysfunctions, a statistically significant difference was seen in GDS-15 scores between both groups. Furthermore, treatment with ω-3 PUFAs was clinically more effective in treating depression in comparison with the placebo. In this study, low-dose ω-3 PUFAs had some efficacy in thetreatment of mild to moderate depression in elderly participants.

Source
Tajalizadekhoob Y, et al. The effect of low-dose omega 3 fatty acids on the treatment of mild to moderate depression in the elderly: a double-blind, randomized, placebo-controlled study. eur Arch Psychiatry Clin Neurosci. 2011 Feb 12. [Epub ahead of print

Red blood cell omega 3 fatty acid levels and markers of accelerated brain aging

ABSTRACT
OBJECTIVE:
Higher dietary intake and circulating levels of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) have been related to a reduced risk for dementia, but the pathways underlying this association remain unclear. We examined the cross-sectional relation of red blood cell (RBC) fatty acid levels to subclinical imaging and cognitive markers of dementia risk in a middle-aged to elderly community-based cohort.

METHODS:

We related RBC DHA and EPA levels in dementia-free Framingham Study participants (n = 1575; 854 women, age 67 ± 9 years) to performance on cognitive tests and to volumetric brain MRI, with serial adjustments for age, sex, and education (model A, primary model), additionally for APOE ε4 and plasma homocysteine (model B), and also for physical activity and body mass index (model C), or for traditional vascular risk factors (model D).

RESULTS:
Participants with RBC DHA levels in the lowest quartile (Q1) when compared to others (Q2-4) had lower total brain and greater white matter hyperintensity volumes (for model A: β ± SE = -0.49 ± 0.19; p = 0.009, and 0.12 ± 0.06; p = 0.049, respectively) with persistence of the association with total brain volume in multivariable analyses. Participants with lower DHA and ω-3 index (RBC DHA+EPA) levels (Q1 vs. Q2-4) also had lower scores on tests of visual memory (β ± SE = -0.47 ± 0.18; p = 0.008), executive function (β ± SE = -0.07 ± 0.03; p = 0.004), and abstract thinking (β ± SE = -0.52 ± 0.18; p = 0.004) in model A, the results remaining significant in all models.

CONCLUSION:
Lower RBC DHA levels are associated with smaller brain volumes and a "vascular" pattern of cognitive impairment even in persons free of clinical dementia.

Source
Tan Zs, Harris WS, Beiser AS et. al. Red blood cell omega 3 fatty acid levels and markers of accelerated brain aging. Neurology 2012:78(9):658-64.

Vitamin B12, cognition, and brain MRI measures: A crosssectional examination

ABSTRACT
OBJECTIVE:

To investigate the interrelations of serum vitamin B12 markers with brain volumes, cerebral infarcts, and performance in different cognitive domains in a biracial population sample cross-sectionally.

Methods:

In 121 community-dwelling participants of the Chicago Health and Aging Project, serum markers of vitamin B12 status were related to summary measures of neuropsychological tests of 5 cognitive domains and brain MRI measures obtained on average 4.6 years later among 121 older adults.

RESULTS:

Concentrations of all vitamin B12–related markers, but not serum vitamin B12 itself, were associated with global cognitive function and with total brain volume. Methylmalonate levels were associated with poorer episodic memory and perceptual speed, and cystathionine and 2-methylcitrate with poorer episodic and semantic memory. Homocysteine concentrations were associated with decreased total brain volume. The homocysteine-global cognition effect was modified and no longer statistically significant with adjustment for white matter volume or cerebral infarcts. The methylmalonate-global cognition effect was modified and no longer significant with adjustment for total brain volume.

CONCLUSIONS:

Methylmalonate, a specific marker of B12 deficiency, may affect cognition by reducing total brain volume whereas the effect of homocysteine (nonspecific to vitamin B12 deficiency) on cognitive performance may be mediated through increased white matter hyperintensity and cerebral infarcts. Vitamin B12 status may affect the brain through multiple mechanisms.

Source
Tangney CC et al. Vitamin B12, cognition, and brain MRI measures: A crosssectional examination. Neurol 77:1276-82, 2011.

DIGESTIVE HEALTH

Optimal vitamin D status for colorectal cancer prevention: a quantitative meta analysis

ABSTRACT
BACKGROUND:
Previous studies, such as the Women's Health Initiative, have shown that a low dose of vitamin D did not protect against colorectal cancer, yet a meta-analysis indicates that a higher dose may reduce its incidence.

METHODS:

Five studies of serum 25(OH)D in association with colorectal cancer risk were identified using PubMed. The results of all five serum studies were combined using standard methods for pooled analysis. The pooled results were divided into quintiles with median 25(OH)D values of 6, 16, 22, 27, and 37 ng/mL. Odds ratios were calculated by quintile of the pooled data using Peto's Assumption-Free Method, with the lowest quintile of 25(OH)D as the reference group. A dose-response curve was plotted based on the odds for each quintile of the pooled data. Data were abstracted and analyzed in 2006.

RESULTS:
Odds ratios for the combined serum 25(OH)D studies, from lowest to highest quintile, were 1.00, 0.82, 0.66, 0.59, and 0.46 (p(trend)<0.0001) for colorectal cancer. According to the DerSimonian-Laird test for homogeneity of pooled data, the studies were homogeneous (chi(2)=1.09, df=4, p=0.90. The pooled odds ratio for the highest quintile versus the lowest was 0.49 (p<0.0001, 95% confidence interval, 0.35-0.68). A 50% lower risk of colorectal cancer was associated with a serum 25(OH)D level > or =33 ng/mL, compared to < or =12 ng/mL.

CONCLUSIONS:
The evidence to date suggests that daily intake of 1000-2000 IU/day of vitamin D(3) could reduce the incidence of colorectal with minimal risk.

Source
Gorham ED, et al. Optimal vitamin D status for colorectal cancer prevention: a quantitative meta analysis. Am J Prev Med. 2007 Mar;32(3):210-6.

Vegetables, Fruit, and Colon Cancer in the Iowa Women's Health Study

ABSTRACT
Previous epidemiologic studies have shown an inverse association between vegetable and fruit consumption and colon cancer risk; few of these studies have been prospective or have focused on women. This report describes results from a prospective cohort study of 41,837 women aged 55-69 years who completed a 127-item food frequency questionnaire in 1986 and were monitored for cancer incidence for 5 years via the State Health Registry of Iowa. After specific exclusion criteria were applied, 212 colon cancer cases and 167,447 person-years were available for analysis. Intakes of 15 vegetable and fruit groups and dietary fiber were the major factors of interest. Consumption of garlic was inversely associated with risk, with an age- and energy-adjusted relative risk of 0.68 (95% confidence interval (CI) 0.46-1.02) for the uppermost versus the lowermost consumption levels. Inverse associations were also observed for intakes of all vegetables and dietary fiber; age- and energy-adjusted relative risks for the uppermost versus the low-

ermost intake quartiles were 0.73 (95% CI 0.47-1.13) and 0.80 (95% CI 0.49-1.31), respectively. Associations for the other vegetable and fruit groups were less remarkable.

Source
Steinmetz KA, et al. Vegetables, Fruit, and Colon Cancer in the Iowa Women's Health Study. Am J Epid. 1994; 163: 232-235

EYE HEALTH

Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8

ABSTRACT

BACKGROUND:
Observational and experimental data suggest that antioxidant and/or zinc supplements may delay progression of age-related macular degeneration (AMD) and vision loss.

OBJECTIVE:
To evaluate the effect of high-dose vitamins C and E, beta carotene, and zinc supplements on AMD progression and visual acuity.

DESIGN:
The Age-Related Eye Disease Study, an 11-center double-masked clinical trial, enrolled participants in an AMD trial if they had extensive small drusen, intermediate drusen, large drusen, noncentral geographic atrophy, or pigment abnormalities in 1 or both eyes, or advanced AMD or vision loss due to AMD in 1 eye. At least 1 eye had best-corrected visual acuity of 20/32 or better. Participants were randomly assigned to receive daily oral tablets containing: (1) antioxidants (vitamin C, 500 mg; vitamin E, 400 IU; and beta carotene, 15 mg); (2) zinc, 80 mg, as zinc oxide and copper, 2 mg, as cupric oxide; (3) antioxidants plus zinc; or (4) placebo.

MAIN OUTCOME MEASURES:
(1) Photographic assessment of progression to or treatment for advanced AMD and (2) at least moderate visual acuity loss from baseline (> or =15 letters). Primary analyses used repeated-measures logistic regression with a significance level of.01, unadjusted for covariates. Serum level measurements, medical histories, and mortality rates were used for safety monitoring.

RESULTS:
Average follow-up of the 3640 enrolled study participants, aged 55-80 years, was 6.3 years, with 2.4% lost to follow-up. Comparison with placebo demonstrated a statistically significant odds reduction for the development of advanced AMD with antioxidants plus zinc (odds ratio [OR], 0.72; 99% confidence interval [CI], 0.52-0.98). The ORs for zinc alone and antioxidants alone are 0.75 (99% CI, 0.55-1.03) and 0.80 (99% CI, 0.59-1.09), respectively. Participants with extensive small drusen, nonextensive intermediate size drusen, or pigment abnormalities had only a 1.3% 5-year probability of progression to advanced AMD. Odds reduction estimates increased when these 1063 participants were excluded (antioxidants plus zinc: OR, 0.66; 99% CI, 0.47-0.91; zinc: OR, 0.71; 99% CI, 0.52-0.99; antioxidants: OR, 0.76; 99% CI, 0.55-1.05). Both zinc and antioxidants plus zinc significantly reduced the odds of developing advanced AMD in this higher-risk group. The only statistically significant reduction in rates of at least moderate visual acuity loss occurred in persons assigned to receive antioxidants plus zinc (OR, 0.73; 99% CI, 0.54-0.99). No statistically significant serious adverse effect was associated with any of the formulations.

CONCLUSIONS:
Persons older than 55 years should have dilated eye examinations to determine their risk of developing advanced AMD. Those with extensive intermediate size drusen, at least 1 large druse, noncentral geographic atrophy in 1 or both eyes, or advanced AMD or vision loss due to AMD in 1 eye, and without contraindications such as smoking, should consider taking a supplement of antioxidants plus zinc such as that used in this study.

Source
Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophth

Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A

ABSTRACT

OBJECTIVE:
To determine whether lutein supplementation will slow visual function decline in patients with retinitis pigmentosa receiving vitamin A.

DESIGN:
Randomized, controlled, double-masked trial of 225 nonsmoking patients, aged 18 to 60 years, evaluated over a 4-year interval. Patients received 12 mg of lutein or a control tablet daily. All were given 15,000 IU/d of vitamin A palmitate. Randomization took into account genetic type and baseline serum lutein level.

MAIN OUTCOME MEASURES:
The primary outcome was the total point score for the Humphrey Field Analyzer (HFA) 30-2 program; prespecified secondary outcomes were the total point scores for the 60-4 program and for the 30-2 and 60-4 programs combined, 30-Hz electroretinogram amplitude, and
Early Treatment Diabetic Retinopathy Study acuity.

RESULTS:
No significant difference in rate of decline was found between the lutein plus vitamin A and control plus vitamin A groups over a 4-year interval for the HFA 30-2 program. For the HFA 60-4 program, a decrease in mean rate of sensitivity loss was observed in the lutein plus vitamin A group (P = .05).

Mean decline with the 60-4 program was slower among those with the highest serum lutein level or with the highest increase in macular pigment optical density at follow-up (P = .01 and P = .006, respectively). Those with the highest increase in macular pigment optical density also had the slowest decline in HFA 30-2 and 60-4 combined field sensitivity (P = .005). No significant toxic effects of lutein supplementation were observed.

CONCLUSION:
Lutein supplementation of 12 mg/d slowed loss of midperipheral visual field on average among nonsmoking adults with retinitis pigmentosa taking vitamin A. Application to Clinical Practice Data are presented that support use of 12 mg/d of lutein to slow visual field loss among nonsmoking adults with retinitis pigmentosa taking vitamin A.

Source
Berson EL, et al. Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A. Arch Ophthalmol. 2010 Apr;128(4):403-11.

Fatty acids and retinopathy

SUMMARY
Dr. Emily Chew (MD) from the US National Institute of Health reviewed the mechanism by which omega-3 fatty acids protect from age-related eye disease (age-related macular degeneration, retinopathy and diabetic retinopathy). She concluded that taking an omega-3 supplement to prevent the disease or slow its rate of progression may prove a better course of action than the current, often painful therapies. As evidence for this, she cited an article in the February 09, 2011 edition of Science Translational Medicine (2) co-authored by SAB member Dr. Arianna Carughi, in which the human clinical evidence component was drawn in part from our 2009 clinical trial on Salmon Oil Plus.

Source
Chew EY, Fatty acids and retinopathy. new england Journal of Medicine, 2011; 364:1970

Dietary n-3 fatty acids and fish intake and incident Age-related Macular Degeneration in women. archives of ophthalmology

ABSTRACT
OBJECTIVE:
To examine whether intake of ω-3 fatty acids and fish affects incidence of age-related macular degeneration (AMD) in women.

DESIGN:
A detailed food-frequency questionnaire was administered at baseline among 39 876 female health professionals (mean [SD] age: 54.6 [7.0] years). A total of 38 022 women completed the questionnaire and were free of a diagnosis of AMD. The main outcome measure was incident AMD responsible for a reduction in best-corrected visual acuity to 20/30 or worse based on self-report confirmed by medical record review.

RESULTS:
A total of 235 cases of AMD, most characterized by some combination of drusen and retinal pigment epithelial changes, were confirmed during an average of 10 years of follow-up. Women in the highest tertile of intake for docosahexaenoic acid, compared with those in the lowest, had a multivariate-adjusted relative risk of AMD of 0.62 (95% confidence interval, 0.44-0.87). For eicosapentaenoic acid, women in the highest tertile of intake had a relative risk of 0.66 (95% confidence interval, 0.48-0.92). Consistent with the findings for docosahexaenoic acid and eicosapentaenoic acid, women who consumed 1 or more servings of fish per week, compared with those who consumed less than 1 serving per month, had a relative risk of AMD of 0.58 (95% confidence interval, 0.38-0.87).

CONCLUSION:
These prospective data from a large cohort of female health professionals without a diagnosis of AMD at baseline indicate that regular consumption of docosahexaenoic acid and eicosapentaenoic acid and fish was associated with a significantly decreased risk of incident AMD and may be of benefit in primary prevention of AMD.

Source
Christen WG, et al. Dietary n-3 fatty acids and fish intake and incident Age-related Macular Degeneration in women. archives of ophthalmology. 2011; 129(7): 921-929. doi:10/1001/archopaphthmol.2011.34

Inflammatory cells during wound repair: the good, the bad and the ugly

ABSTRACT
Damage to any tissue triggers a cascade of events that leads to rapid repair of the wound - if the tissue is skin, then repair involves re-epithelialization, formation of granulation tissue and contraction of underlying wound connective tissues. This concerted effort by the wounded cell layers is accompanied by, and might also be partially regulated by, a robust inflammatory response, in which first neutrophils and then macrophages and mast cells emigrate from nearby tissues and from the circulation. Clearly, this inflammatory response is crucial for fighting infection and must have been selected for during the course of evolution so that tissue damage did not inevitably lead to death through septicemia. But, aside from this role, exactly what are the functions of the various leukocyte lineages that are recruited with overlapping time courses to the wound site, and might they do more harm than good? Recent knockout and knockdown studies suggest that depletion of one or more of the inflammatory cell lineages can even enhance healing, and we discuss new views on how regulation of the migration of inflammatory cells to sites of tissue damage might guide therapeutic strategies for modulating the inflammatory response.

Source
Martin P, et al. Inflammatory cells during wound repair: the good, the bad and the ugly. Trends Cell Biol. 2005 Nov;15(11):599-607.

Vitamin D status and early age related macular degeneration in postmenopausal women. archives of ophthalmology

ABSTRACT

OBJECTIVE:

The relationship between serum 25-hydroxyvitamin D (25[OH]D) concentrations (nmol/L) and the prevalence of early age-related macular degeneration (AMD) was investigated in participants of the Carotenoids in Age-Related Eye Disease Study.

METHODS:

Stereoscopic fundus photographs, taken from 2001 to 2004, assessed AMD status. Baseline (1994-1998) serum samples were available for 25(OH)D assays in 1313 women with complete ocular and risk factor data. Odds ratios (ORs) and 95% confidence intervals (CIs) for early AMD (n = 241) of 1287 without advanced disease were estimated with logistic regression and adjusted for age, smoking, iris pigmentation, family history of AMD, cardiovascular disease, diabetes, and hormone therapy use.

RESULTS:

In multivariate models, no significant relationship was observed between early AMD and 25(OH)D (OR for quintile 5 vs 1, 0.79; 95% CI, 0.50-1.24; P for trend = .47). A significant age interaction (P = .002) suggested selective mortality bias in women aged 75 years and older: serum 25(OH)D was associated with decreased odds of early AMD in women younger than 75 years (n = 968) and increased odds in women aged 75 years or older (n = 319) (OR for quintile 5 vs 1, 0.52; 95% CI, 0.29-0.91; P for trend = .02 and OR, 1.76; 95% CI, 0.77-4.13; P for trend = .05, respectively). Further adjustment for body mass index and recreational physical activity, predictors of 25(OH)D, attenuated the observed association in women younger than 75 years. Additionally, among women younger than 75 years, intake of vitamin D from foods and supplements was related to decreased odds of early AMD in multivariate models; no relationship was observed with self-reported time spent in direct sunlight.

CONCLUSIONS:

High serum 25(OH)D concentrations may protect against early AMD in women younger than 75 years.

Source

Millen AE, et al. Vitamin D status and early age related macular degeneration in postmenopausal women. archives of ophthalmology. 2011; 129(4): 481:489. doi:10.1001/archophthalmol.2011.48

Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial

ABSTRACT

BACKGROUND:

A suboptimal vitamin D and calcium status has been associated with higher risk of type 2 diabetes in observational studies, but evidence from trials is lacking.

OBJECTIVE:

We determined whether vitamin D supplementation, with or without calcium, improved glucose homeostasis in adults at high risk of diabetes.

DESIGN:

Ninety-two adults were randomly assigned in a 2-by-2 factorial-design, double-masked, placebo-controlled trial to receive either cholecalciferol (2000 IU once daily) or calcium carbonate (400 mg twice daily) for 16 wk. The primary outcome was the change in pancreatic β cell function as measured by the disposition index after an intravenous-glucose-tolerance test. Other outcomes were acute insulin response, insulin sensitivity, and measures of glycemia.

RESULTS:

Participants had a mean age of 57 y, a body mass index (BMI; in kg/m(2)) of 32, and glycated hemoglobin (Hb A(1c)) of 5.9%. There was no significant vitamin D × calcium interaction on any outcomes. The disposition index increased in the vitamin D group and decreased in the no-vitamin D group (adjusted mean change ± SE: 300 ± 130 compared with -126 ± 127, respectively; P = 0.011), which was explained by an improvement in insulin secretion (62 ± 39 compared with -36 ± 37 mU · L(-1) · min, respectively; P = 0.046). Hb A(1c) increased less, but nonsignificantly, in the vitamin D group than in the no-vitamin D group (0.06 ± 0.03% compared with 0.14 ± 0.03%, respectively; P = 0.081). There was no significant difference in any outcomes with calcium compared with no calcium.

CONCLUSION:

In adults at risk of type 2 diabetes, short-term supplementation with cholecalciferol improved β cell function and had a marginal effect on attenuating the rise in Hb A(1c).

Source

Mitri J et al. Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. Am J

Biological role of lutein in the light induced retinal degeneration

ABSTRACT

Lutein, a xanthophyll of a carotenoid, is anticipated as a therapeutic product to prevent human eye diseases. However, its biological mechanism is still unclear. Here, we show the molecular mechanism of lutein's effect to reduce photodamage of the retina. We analyzed the light-exposed retinas of Balb/c mice given lutein-supplemented or normal diet. Visual function was measured by electroretinogram, and histological changes were observed. Immunohistochemical and immunoblot analyses were performed to analyze molecular mechanism. The reactive oxygen species induced in the retina was evaluated by fluorescent probes. In the mice after light

exposure, reduction of a-wave and b-wave amplitudes in electroretinogram, indicating visual impairment, and thinning of the photoreceptor cell layer owing to apoptosis were both attenuated by lutein diet. Interestingly, γ-H2AX, a marker for double-strand breaks (DSBs) in DNA, was up-regulated in the photoreceptor cells after light exposure, but this increase was attenuated by lutein diet, suggesting that DSBs caused by photodamage contributed to the photoreceptor cell death and that this change was suppressed by lutein. Moreover, the expression of eyes absent (EYA), which promotes DNA repair and cell survival, was significantly up-regulated with lutein diet in the light-exposed retina. Therefore, lutein induced EYA for DNA repair, which could suppress DNA damage and photoreceptor cell apoptosis. Lutein reduced light-induced oxidative stress in the retina, which might contribute to promote DNA repair. The lutein-supplemented diet attenuated light-induced visual impairment by protecting the photoreceptor cells' DNA.

Source
Sasaki M., Biological role of lutein in the light induced retinal degeneration. Journal of nutritional Biochemistry. 2011; doi:10.1016/j.jnutbio.2011.01.006

HEALTHY PREGNANCY

Vitamin D and gestational diabetes mellitus

ABSTRACT
The incidence of gestational diabetes mellitus (GDM) is increasing worldwide. GDM can be responsible for an important proportion of adverse fetal and maternal outcomes during pregnancy, and it is associated with long-term health deterioration for both mother and child. Therefore, it is important to identify potentially modifiable risk factors for GDM. Accumulating evidence links vitamin D deficiency with abnormal glucose metabolism, and epidemiological studies have shown that women who develop GDM are more likely to be vitamin D deficient. This review discusses the prevalence, risk factors, and outcomes of GDM and vitamin D deficiency in pregnant women, outlines the possible mechanism of action of vitamin D in glucose homeostasis, and summarizes emerging evidence that associates vitamin D deficiency with the risk of developing GDM. This critical review of the literature indicates there is a need for intervention trials to test the possible beneficial effect of vitamin D supplementation in pregnant women with low vitamin D status to reduce the risk of developing GDM.

Source
Alzaim M, Wood RJ. Vitamin D and gestational diabetes mellitus. Nutr Rev. 2013 Mar;71(3):158-67.

Periconceptional multivitamin use and infant birth weight disparities.

ABSTRACT
PURPOSE:
In the United States, African American women deliver preterm and low birth weight infants two to three times more frequently than their white counterparts. Our objective was to determine whether maternal periconceptional multivitamin (MVI) use is associated with this disparity.

METHODS:
As a secondary analysis of previously collected data from mothers of non-malformed infants from the Slone Epidemiology Center Birth Defects Study, we conducted a retrospective cohort study of 2331 non-Hispanic white and 133 non-Hispanic black mother/infant pairs from 1998 through 2007. To estimate the effect of MVI use on birth outcomes, linear regression models were used.

RESULTS:
In white subjects, MVI use was not associated with birth weight, gestational age, or weight-for-gestational-age. However, in black subjects, MVI use was associated with a 536-gram increased birth weight (p=0.001). Black MVI users also had longer gestations (although not statistically significant). When birth weights were adjusted for gestational age using z scores, MVI use was associated with increased fetal growth in black infants (+0.86 z score units, 95% confidence interval: 0.35-1.36).

CONCLUSIONS:
The present findings suggest MVI use may improve fetal growth and possibly gestational age in the offspring of African American women.

Source
Burris HH, et al. Periconceptional multivitamin use and infant birth weight disparities. Ann Epidemiol. 2010 Mar;20(3):233-40.

Antenatal and Postnatal Iron Supplementation and Childhood Mortality in Rural Nepal: A Prospective Follow-up in a Randomized, controlled Community Trial

ABSTRACT
The long-term benefits of antenatal iron supplementation in child survival are not known. In 1999-2001, 4,926 pregnant women in rural Nepal participated in a cluster-randomized, double-masked, controlled trial involving 4 alternative combinations of micronutrient supplements, each containing vitamin A. The authors examined the impact on birth weight and early infant mortality in comparison with controls, who received vitamin A only. They followed the surviving offspring of these women at approximately age 7 years to study effects of in utero supplementation on survival. Of 4,130 livebirths, 209 infants died in the first 3 months and 8 were lost to follow-up. Of those remaining, 3,761 were followed, 150 died between ages 3 months and 7 years, and 152 were lost to follow-up. Mortality rates per 1,000 child-years from birth to age 7 years differed by maternal supplementation group, as follows: folic acid, 13.4; folic acid-iron, 10.3; folic acid-iron-zinc, 12.0; multiple

micronutrients; 14.0; and controls, 15.2. Hazard ratios were 0.90 (95% confidence interval (CI): 0.65, 1.22), 0.69 (95% CI: 0.49, 0.99), 0.80 (95% CI: 0.58, 1.11), and 0.93 (95% CI: 0.66, 1.31), respectively, in the 4 supplementation groups. Maternal iron-folic acid supplementation reduced mortality among these children by 31% between birth and age 7 years. These results provide additional motivation for strengthening antenatal iron-folic acid programs.

Source
Christian P, et al. Antenatal and Postnatal Iron Supplementation and Childhood Mortality in Rural Nepal: A Prospective Follow-up in a Randomized, controlled Community Trial. am J of epid. 2009 Sep;170 (9): 1127-1136.

Omega-3 fatty acids and pregnancy

ABSTRACT
Omega-3 fatty acids are essential fatty acids that must be consumed in the diet. Adequate consumption of omega-3 fatty acids is vitally important during pregnancy as they are critical building blocks of fetal brain and retina. Omega-3 fatty acids may also play a role in determining the length of gestation and in preventing perinatal depression. The most biologically active forms of omega-3 fatty acids are docosahexaenoic acid and eicosapentaenoic acid, which are primarily derived from marine sources such as seafood and algae. Recent surveys, however, indicate that pregnant women in the United States and in other countries eat little fish and therefore do not consume enough omega-3 fatty acids, primarily due to concern about the adverse effects of mercury and other contaminants on the developing fetus. This review discusses the benefits of omega-3 fatty acid consumption during pregnancy and provides guidelines for obstetricians advising patients.

Source
Coletta JM et al. Omega-3 fatty acids and pregnancy. Rev Obstet Gynecol 3:163-71, 2010.

Prenatal fatty acid status and child adiposity at age 3 y: results from a US pregnancy cohort

ABSTRACT
BACKGROUND:
Exposure to polyunsaturated fatty acids (PUFAs) in early life may influence adiposity development.

OBJECTIVE:
We examined the extent to which prenatal n-3 (omega-3) and n-6 (omega-6) PUFA concentrations were associated with childhood adiposity.

DESIGN:
In mother-child pairs in the Project Viva cohort, we assessed midpregnancy fatty acid intakes (n = 1120), maternal plasma PUFA concentrations (n = 227), and umbilical cord plasma PUFA concentrations (n = 302). We performed multivariable regression analyses to examine independent associations of n-3 PUFAs, including docosahexaenoic and eicosapentaenoic acids (DHA + EPA), n-6 PUFAs, and the ratio of n-6:n-3 PUFAs, with child adiposity at age 3 y measured by the sum of subscapular and triceps skinfold thicknesses (SS + TR) and risk of obesity (body mass index ≥95th percentile for age and sex).

RESULTS:
Mean (±SD) DHA + EPA intake was 0.15 ± 0.14 g DHA + EPA/d, maternal plasma concentration was 1.9 ± 0.6%, and umbilical plasma concentration was 4.6 ± 1.2%. In children, SS + TR was 16.7 ± 4.3 mm, and 9.4% of children were obese. In the adjusted analysis, there was an association between each SD increase in DHA + EPA and lower child SS + TR [-0.31 mm (95% CI: -0.58, -0.04 mm) for maternal diet and -0.91 mm (95% CI: -1.63, -0.20 mm) for cord plasma] and lower odds of obesity [odds ratio (95% CI): 0.68 (0.50, 0.92) for maternal diet and 0.09 (0.02, 0.52) for cord plasma]. Maternal plasma DHA + EPA concentration was not significantly associated with child adiposity. A higher ratio of cord plasma n-6:n-3 PUFAs was associated with higher SS + TR and odds of obesity.

CONCLUSION:
An enhanced maternal-fetal n-3 PUFA status was associated with lower childhood adiposity.

Source
Donahue SM, et al. Prenatal fatty acid status and child adiposity at age 3 y: results from a US pregnancy cohort. am J clin nutr. 2011 Feb 10. [Epub ahead of print]

Dietary PUFA for preterm and term infants: review of clinical studies

ABSTRACT
Human milk contains n-3 and n-6 LCPUFA (long chain polyunsaturated fatty acids), which are absent from many infant formulas. During neonatal life, there is a rapid accretion of AA (arachidonic acid) and DHA (docosahexaenoic acid) in infant brain, DHA in retina and of AA in the whole body. The DHA status of breast-fed infants is higher than that of formula-fed infants when formulas do not contain LCPUFA. Studies report that visual acuity of breast-fed infants is better than that of formula-fed infants, but other studies do not find a difference. Cognitive development of breast-fed infants is generally better, but many sociocultural confounding factors may also contribute to these differences. The effect of dietary LCPUFA on FA status, immune function, visual, cognitive, and motor functions has been evaluated in preterm and term infants. Plasma and RBC FA status of infants fed formulas supplemented with both n-3 and n-6 LCPUFA was closer to the status of breast-fed infants than to that of infants fed formulas containing no LCPUFA. Adding n-3 LCPUFA to preterm-infant formulas led to initial beneficial effects on visual acuity. Few data are available on cognitive function, but it seems that in preterm infants, feeding n-3 LCPUFA improved visual atten-

tion and cognitive development compared with infants receiving no LCPUFA. Term infants need an exogenous supply of AA and DHA to achieve similar accretion of fatty acid in plasma and RBC (red blood cell) in comparison to breast-fed infants. Fewer than half of all studies have found beneficial effects of LCPUFA on visual, mental, or psychomotor functions. Improved developmental scores at 18 mo of age have been reported for infants fed both AA and DHA. Growth, body weight, and anthropometrics of preterm and term infants fed formulas providing both n-3 and n-6 LCPUFA fatty acids is similar in most studies to that of infants fed formulas containing no LCPUFA. A larger double-blind multicenter randomized study has recently demonstrated improved growth and developmental scores in a long-term feeding study of preterm infants. Collectively, the body of literature suggests that LCPUFA is important to the growth and development of infants. Thus, for preterm infants we recommend LCPUFA intakes in the range provided by feeding of human milk typical of mothers in Western countries. This range can be achieved by a combination of AA and DHA, providing an AA to DHA ratio of approximately 1.5 and a DHA content of as much as 0.4%. Preterm infants may benefit from slightly higher levels of these fatty acids than term infants. In long-term studies, feeding more than 0.2% DHA and 0.3% AA improved the status of these fatty acids for many weeks after DHA; AA was no longer present in the formula, enabling a DHA and AA status more similar to that of infants fed human milk. The addition of LCPUFA in infant formulas for term infants, with appropriate regard for quantitative and qualitative qualities, is safe and will enable the formula-fed infant to achieve the same blood LCPUFA status as that of the breast-fed infant.

Source
Fleith M, Clandinin MT. Dietary PUFA for preterm and term infants: review of clinical studies. Crit Rev Food Sci Nutr. 2005;45(3):205-29

Omega-3 Acid supplementation during pregnancy

ABSTRACT
Omega-3 fatty acids are essential and can only be obtained from the diet. The requirements during pregnancy have not been established, but likely exceed that of a non-pregnant state. Omega-3 fatty acids are critical for fetal neurodevelopment and may be important for the timing of gestation and birth weight as well. Most pregnant women likely do not get enough omega-3 fatty acids because the major dietary source, seafood, is restricted to 2 servings a week. For pregnant women to obtain adequate omega-3 fatty acids, a variety of sources should be consumed: vegetable oils, 2 low-mercury fish servings a week, and supplements (fish oil or algae-based docosahexaenoic acid).

Source
Greenberg JA et al. Omega-3 Acid supplementation during pregnancy. Rev Obstet Gynecol 1:162–69, 2008.

Prenatal docosahexaenoic acid supplementation and infant morbidity: randomized controlled trial

ABSTRACT
OBJECTIVE:
Long-chain polyunsaturated fatty acids such as docosahexaenoic acid (DHA) influence immune function and inflammation; however, the influence of maternal DHA supplementation on infant morbidity is unknown. We investigated the effects of prenatal DHA supplementation on infant morbidity.

METHODS:
In a double-blind randomized controlled trial conducted in Mexico, pregnant women received daily supplementation with 400 mg of DHA or placebo from 18 to 22 weeks' gestation through parturition. In infants aged 1, 3, and 6 months, caregivers reported the occurrence of common illness symptoms in the preceding 15 days.

RESULTS:
Data were available at 1, 3, and 6 months for 849, 834, and 834 infants, respectively. The occurrence of specific illness symptoms did not differ between groups; however, the occurrence of a combined measure of cold symptoms was lower in the DHA group at 1 month (OR: 0.76; 95% CI: 0.58–1.00). At 1 month, the DHA group experienced 26%, 15%, and 30% shorter duration of cough, phlegm, and wheezing, respectively, but 22% longer duration of rash (all $P \leq .01$). At 3 months, infants in the DHA group spent 14% less time ill ($P < .0001$). At 6 months, infants in the DHA group experienced 20%, 13%, 54%, 23%, and 25% shorter duration of fever, nasal secretion, difficulty breathing, rash, and "other illness," respectively, but 74% longer duration of vomiting (all $P < .05$).

CONCLUSIONS:
DHA supplementation during pregnancy decreased the occurrence of colds in children at 1 month and influenced illness symptom duration at 1, 3, and 6 months.

Source
Imhoff-Kunsch B, Stein AD, Martorell R et al. Prenatal docosahexaenoic acid supplementation and infant morbidity: randomized controlled trial. Pediatrics.2011; 128(3):505-12.

World Association of Perinatal Medicine Dietary Guidelines Working Group: The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations

ABSTRACT
This paper reviews current knowledge on the role of the long-chain polyunsaturated fatty acids (LC-PUFA), docosahexaenoic acid (DHA, C22:6n-3) and arachidonic acid (AA, 20:4n-6), in maternal and term infant nutrition as well as infant development. Consensus recommendations and practice guidelines for health-care providers sup-

ported by the World Association of Perinatal Medicine, the Early Nutrition Academy, and the Child Health Foundation are provided. The fetus and neonate should receive LC-PUFA in amounts sufficient to support optimal visual and cognitive development. Moreover, the consumption of oils rich in n-3 LC-PUFA during pregnancy reduces the risk for early premature birth. Pregnant and lactating women should aim to achieve an average daily intake of at least 200 mg DHA. For healthy term infants, we recommend and fully endorse breastfeeding, which supplies preformed LC-PUFA, as the preferred method of feeding. When breastfeeding is not possible, we recommend use of an infant formula providing DHA at levels between 0.2 and 0.5 weight percent of total fat, and with the minimum amount of AA equivalent to the contents of DHA. Dietary LC-PUFA supply should continue after the first six months of life, but currently there is not sufficient information for quantitative recommendations.

Source
Koletzko B, Lien E, Agostoni C, et al. World Association of Perinatal Medicine Dietary Guidelines Working Group: The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendat

Folate recommendations for pregnancy, lactation, and infancy

ABSTRACT
An adequate intake of folate during pregnancy, lactation, and infancy is essential for maternal and child health and normal growth. Higher folate requirements during pregnancy and lactation are difficult to meet by increased intake of folate-rich food products only. Supplementation with folic acid is recommended not only to meet the higher requirements but also to prevent adverse pregnancy outcomes such as neural tube defects (NTDs). In countries that have implemented food fortification with folic acid, the folate intake has raised but does not yet meet the recommended amount for NTD risk reduction. Women's awareness of the need to supplement with folic acid prior to conception shall be raised in all countries. It is under debate whether a high folic acid intake might have metabolic and functional effects in utero and for the infant. Research is needed to investigate potential alternative folate forms for food fortification programs and to test their efficacy in risk reduction of adverse pregnancy outcomes. Breast-fed infants most likely receive sufficient folate. While the folate level of human milk is simulated in infant formula, data are lacking on the bioavailability and effect of folic acid in infants and on whether a tolerable upper intake level should be defined.

Source
Lamers Y (2011). Folate recommendations for pregnancy, lactation, and infancy. Ann Nutr Metab 59(1): 32-37.

Folate and neural tube defects

ABSTRACT
A protective effect of folate against the development of neural tube defects (NTDs), specifically, anencephaly and spina bifida, is now well recognized, having been established by a chain of clinical research studies over the past half century. This article summarizes the more important of these studies, which have led to the current situation in which all women capable of becoming pregnant are urged to ingest folic acid regularly. The recommended intakes are 4 mg/d for those at high risk (by virtue of a previous NTD pregnancy outcome) and 0.4 mg/d for all others. However, a reduction in NTD births did not follow promulgation of these recommendations, and so folic acid fortification was mandated in the United States and some other countries. Although some controversy remains about the adequacy of fortification levels, the process was followed by significant improvement in folate indexes and a reduction of 25-30% in NTD frequency (about one-half of the proportion of cases assumed to be responsive to folate). The folate-NTD relation represents the only instance in which a congenital malformation can be prevented simply and consistently. Nevertheless, several research gaps remain: identification of the mechanism by which the defect occurs and how folate ameliorates it; characterization of the relative efficacy of food folate, folic acid added to foods, and folic acid by itself; delineation of the dose-response relations of folate and NTD prevention; and more precise quantification of the dose needed to prevent recurrences.

Source
Pitkin RM. Folate and neural tube defects. Am J Clin Nutr 2007; 85(1): 285S-288S.

Maternal vitamin D status as a critical determinant in gestational diabetes

ABSTRACT
OBJECTIVE:
To synthesize published research to determine the evidence for the association between maternal vitamin D status during pregnancy and the development of gestational diabetes mellitus (GDM).

DATA SOURCES:
Literature searches were conducted for data based articles that examined maternal vitamin D during pregnancy, GDM, glucose tolerance, and insulin resistance using the PubMed, CINAHL, and SCOPUS data bases and reference lists from reviewed papers.

STUDY SELECTION:
Primary research studies published in the English language between 1999 and 2011 reporting findings regarding the association of vitamin D with glucose homeostasis during pregnancy and GDM.

DATA EXTRACTION:
Study characteristics and findings related to vitamin D status determinants, gestational timing, and measures of glucose homeostasis and insulin resistance.

DATA SYNTHESIS:

Six data based articles met the criteria for study inclusion. Study findings comprised solely Level-2 evidence for the association of maternal vitamin D deficiency and risk of GDM. The majority of studies (66%) were conducted between 24 and 30 weeks gestation. Five (83%) studies reported an inverse relationship between circulating vitamin D levels and markers of glucose homeostasis associated with gestational diabetes or an increased risk for GDM associated with reduced maternal levels of vitamin D. In one study, researchers did not identify an association between vitamin D and GDM but did identify an association between higher vitamin D levels and lower fasting glucose and insulin levels.

CONCLUSION:
Maternal vitamin D deficiency and insufficiency is prevalent among gravid women and is associated with markers of altered glucose homeostasis. These findings underscore the need for mechanistic and clinical studies to determine optimal vitamin D status in pregnancy for reduction in the risk for GDM with implications for vitamin D supplementation as a potential target for GDM prevention.

Source
Senti J, Thiele DK, Anderson CM. Maternal vitamin D status as a critical determinant in gestational diabetes. J Obstet Gynecol Neonatal Nurs. 2012;41(3)L 328-38.

Periconception dietary intake of choline and betaine and neural tube defects in offspring

ABSTRACT
Periconceptional intake of folic acid prevents some neural tube defects (NTDs). Other nutrients may also contribute to NTD etiologies; a likely candidate is choline. Similar to folic acid, choline is involved in one-carbon metabolism for methylation of homocysteine to methionine. The authors investigated whether maternal periconceptional dietary intakes of choline and its metabolite betaine influence NTD risk. Data were derived from a case-control study of fetuses and infants with NTDs among 1989-1991 California births. In-person interviews were conducted with mothers of 424 NTD cases and with mothers of 440 nonmalformed controls. A standard 100-item food frequency questionnaire was used to assess nutrient intake. Dietary intakes of choline were associated with reduced NTD risks. Controlling for intake of supplemental folic acid, dietary folate, dietary methionine, and other covariates did not substantially influence risk estimates for choline. NTD risk estimates were lowest for women whose diets were rich in choline, betaine, and methionine. That is, for women whose intake was above the 75th percentile compared with below the 25th percentile for all three nutrients, the odds ratio was 0.17 (95% confidence interval: 0.04, 0.76). Study findings for dietary components other than folic acid offer additional clues about the complex etiologies of NTDs.

Source
Shaw G et al. Periconception dietary intake of choline and betaine and neural tube defects in offspring. Am J Epidemiol 2004;160-102-109.

Folic Acid Supplementation for the Prevention of Neural Tube Defects: An Update of the Evidence for the U.S. Preventive Services Task Force Rockville (MD): Agency for Healthcare Research and Quality (US)

ABSTRACT
BACKGROUND:
Neural tube defects (NTDs) are among the most common birth defects in the United States.

PURPOSE:
To update the evidence on folic acid supplementation in women of childbearing age for the prevention of neural tube defects in their offspring.

DATA SOURCES:
MEDLINE and Cochrane Library searches (from January 1995 through November 2007), recent systematic reviews, reference lists of retrieved articles, and expert suggestions.

STUDY SELECTION:
English language studies were selected to answer the following two questions: Does folic acid supplementation in women of childbearing age reduce the risk of a pregnancy affected by a neural tube defect? Does folic acid supplementation in women of childbearing age increase the risk of any harmful outcomes for either the woman or the infant? The following study types were selected: for potential benefits of folic acid—randomized, controlled trials (RCTs), case-control studies, cohort studies, systematic reviews and meta-analyses; for potential harms of folic acid—RCTs, case-control studies, systematic reviews, meta-analyses, and large observational studies.

DATA EXTRACTION:
All studies were reviewed, abstracted, and rated for quality using predefined U.S. Preventive Services Task Force criteria.

DATA SYNTHESIS:
Four observational studies reported benefit, in reduction of risk of NTD associated with folic acid-containing supplements. Differences in study type and methods prevent the calculation of a summary of the reduction in risk. The one included study on harms reported that the association of twinning with folic acid intake disappeared after adjusting for in vitro fertilization and for underreporting of folic acid intake.

LIMITATIONS:
There is limited evidence on dose. We found no evidence on the potential harm of masking vitamin B12 deficiency in women of childbearing age. Our search focused on NTDs and therefore does not provide a comprehensive review of the effects of folic acid on all possible outcomes.

CONCLUSIONS:
New observational evidence supports previous RCT evidence that folic acid—containing supplements reduce the risk of NTD-affected pregnancies. The association of

folic acid use with twin gestation may be confounded by fertility interventions including ovulation simulation and in vitro fertilization.

Source
Wolff T, Witkop CT, Miller T, Syed SB. Folic Acid Supplementation for the Prevention of Neural Tube Defects: An Update of the Evidence for the U.S. Preventive Services Task Force Rockville (MD): Agency for Healthcare Research and Quality (US); 2009 May. R

HEART HEALTH

Impact of omega-3 polyunsaturated fatty acids on coronary plaque instability

ABSTRACT

OBJECTIVE:
To assess the impact of omega-3 polyunsaturated fatty acids (ω3 PUFAs) on coronary plaque instability.

METHODS:
Serum content of eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA) was measured in 336 of 368 consecutive patients suspected of having coronary artery disease who underwent coronary angiography. Conventional and integrated backscatter intravascular ultrasound (IB-IVUS) parameters were analyzed in 116 patients with 128 coronary plaques, using a 43-MHz (motorized pullback 0.5mm/s) intravascular catheter (View It, Terumo Co., Japan). Lipid-rich plaques were classified into two categories according to their components.

RESULTS:
Patients with acute coronary syndrome had significantly lower levels of ω3 PUFAs (especially of EPA and DPA) than those without it. IB-IVUS analyses showed that ω3 PUFAs correlated inversely with % lipid volume and positively with % fibrous volume. Patients with low EPA levels, low DPA levels, and low DHA levels had a significantly higher % lipid volume (p=0.048, p=0.008, and p=0.036, respectively) and a significantly lower % fibrous volume (p=0.035, p=0.008, and p=0.034, respectively) than those with high levels of these fatty acids. Even after adjustment for confounders, the presence of both low EPA and low DPA levels proved to be an independent predictor for lipid-rich plaques in any of the two categories.

CONCLUSIONS:
A lower serum content of ω3 PUFAs (especially of EPA and DPA) was significantly associated with lipid-rich plaques, suggesting the contribution to the incidence of acute coronary syndrome.

Source
Amano T, et al. Impact of omega-3 polyunsaturated fatty acids on coronary plaque instability. Atherosclerosis. 2011 Sep; 218(1):110-6.

Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: a randomized controlled trial

ABSTRACT

BACKGROUND:
Homocysteine is a risk factor for Alzheimer's disease. In the first report on the VITACOG trial, we showed that homocysteine-lowering treatment with B vitamins slows the rate of brain atrophy in mild cognitive impairment (MCI). Here we report the effect of B vitamins oncognitive and clinical decline (secondary outcomes) in the same study.

METHODS:
This was a double-blind, single-centre study, which included participants with MCI, aged ≥ 70 y, randomly assigned to receive a daily dose of 0.8 mg folic acid, 0.5 mg vitamin B(12) and 20 mg vitamin B(6) (133 participants) or placebo (133 participants) for 2 y. Changes in cognitiveor clinical function were analysed by generalized linear models or mixed-effects models.

RESULTS:
The mean plasma total homocysteine was 30% lower in those treated with B vitamins relative to placebo. B vitamins stabilized executive function (CLOX) relative to placebo (P = 0.015). There was significant benefit of B-vitamin treatment among participants with baseline homocysteine above the median (11.3 μmol/L) in global cognition (Mini Mental State Examination, P < 0.001), episodic memory (Hopkins Verbal Learning Test-delayed recall, P = 0.001) and semantic memory (category fluency, P = 0.037). Clinical benefit occurred in the B-vitamin group for those in the upper quartile of homocysteine at baseline in global clinical dementia rating score (P = 0.02) and IQCODE score (P = 0.01).

CONCLUSION:
In this small intervention trial, B vitamins appear to slow cognitive and clinical decline in people with MCI, in particular in those with elevated homocysteine. Further trials are needed to see if this treatment will slow or prevent conversion from MCI to dementia.

Source
de Jager CA et al. Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: a randomized controlled trial. Int J Geriatr Psychiatry [Epub ahead of print, July, 2011]

Dietary choline and betaine intakes in relationship to concentrations of inflammatory markers in healthy adults: the ATTICA study

ABSTRACT

BACKGROUND:
Choline and betaine are found in a variety of plant and animal foods and were recently shown to be associated with decreased

homocysteine concentrations.

OBJECTIVE:
The scope of this work was to investigate the associations between dietary choline and betaine consumption and various markers of low-grade systemic inflammation.

DESIGN:
Under the context of a cross-sectional survey that enrolled 1514 men (18-87 y of age) and 1528 women (18-89 y of age) with no history of cardiovascular disease (the ATTICA Study), fasting blood samples were collected and inflammatory markers were measured. Dietary habits were evaluated with a validated food-frequency questionnaire, and the intakes of choline and betaine were calculated from food-composition tables.

RESULTS:
Compared with the lowest tertile of choline intake (<250 mg/d), participants who consumed >310 mg/d had, on average, 22% lower concentrations of C-reactive protein ($P < 0.05$), 26% lower concentrations of interleukin-6 ($P < 0.05$), and 6% lower concentrations of tumor necrosis factor-alpha ($P < 0.01$). Similarly, participants who consumed >360 mg/d of betaine had, on average, 10% lower concentrations of homocysteine ($P < 0.01$), 19% lower concentrations of C-reactive protein ($P < 0.1$), and 12% lower concentrations of tumor necrosis factor-alpha ($P < 0.05$) than did those who consumed <260 mg/d. These findings were independent of various sociodemographic, lifestyle, and clinical characteristics of the participants.

CONCLUSIONS:
Our results support an association between choline and betaine intakes and the inflammation process in free-eating and apparently healthy adults. However, further studies are needed to confirm or refute our findings.

Source
Detopoulou P et al. Dietary choline and betaine intakes in relationship to concentrations of inflammatory markers in healthy adults: the ATTICA study. Am J Clin Nutr 2008;87:424-430.

Physicians and nurses use and recommend dietary supplements: report of a survey

ABSTRACT
BACKGROUND:
Numerous surveys show that dietary supplements are used by a large proportion of the general public, but there have been relatively few surveys on the prevalence of dietary supplement use among health professionals, including physicians and nurses. Even less information is available regarding the extent to which physicians and nurses recommend dietary supplements to their patients.

METHODS:
An online survey was administered in October 2007 to 900 physicians and 277 nurses by Ipsos Public Affairs for the Council for Responsible Nutrition (CRN), a trade association representing the dietary supplement industry. The health professionals were asked whether they used dietary supplements and their reasons for doing so, and whether they recommend dietary supplements to their patients.

RESULTS:
The "Life...supplemented" Healthcare Professionals Impact Study (HCP Impact Study) found that 72% of physicians and 89% of nurses in this sample used dietary supplements regularly, occasionally, or seasonally. Regular use of dietary supplements was reported by 51% of physicians and 59% of nurses. The most common reason given for using dietary supplements was for overall health and wellness (40% of physicians and 48% of nurses), but more than two-thirds cited more than one reason for using the products. When asked whether they "ever recommend dietary supplements" to their patients, 79% of physicians and 82% of nurses said they did.

CONCLUSION:
Physicians and nurses are as likely as members of the general public to use dietary supplements, as shown by comparing the results of this survey with data from national health and nutrition surveys. Also, most physicians and nurses recommend supplements to their patients, whether or not the clinicians use dietary supplements themselves.

Source
Dickinson A, et al. Physicians and nurses use and recommend dietary supplements: report of a survey. Nutr J. 2009 Jul 1;8:29.

Effect of low carotene diet on malondialdehyde (MDA) concentration

ABSTRACT
OBJECTIVE:
The purpose of the study was to evaluate the effect of a low carotenoid diet (83 micrograms Beta-carotene) on malondialdehyde-thiobarbituric acid (MDA-TBA) concentrations of nine pre-menopausal women.

METHODS:
Subjects lived on the metabolic research unit of the Western Human Nutrition Research Center (WHNRC), where diet, exercise and other activities were controlled. Five subjects (Group C, control group) consumed a low carotenoid diet and received an additional 0.5 mg/day of Beta-carotene while four subjects (Group P, placebo group) received only the low carotenoid diet during days 1 to 60 (period 1). All subjects received 0.5 mg/day of Beta-carotene during days 60 to 100 (period 2), plus three capsules/day mixed carotenoid supplement (Neo-Life Company) during study days 100 to 120. Changes in MDA-TBA concentrations were analyzed during the study periods and between the groups.

RESULTS:
At the start of the study (day 1), no significant difference in the MDA-TBA concentration was observed between the control (Group C) and the placebo (Group P) subjects. During period 1 (days 2 to 60), when Group P subjects consumed the low carotenoid diet without supplementation, the MDA-TBA values for Group P rose markedly and were significantly ($p < 0.05$) higher than the MDA-TBA values for Group C subjects who were receiving carotenoid supplementation. During period 2 (days 60

to 100) when both groups received carotenoid supplementation, the MDA-TBA values of Group P subjects were significantly ($p < 0.05$) reduced to the point where they were similar to the MDA-TBA values for Group C subjects.

CONCLUSIONS:
These findings provide evidence to support the beneficial effects of carotenoids in preventing lipid peroxidation in the cells. Further studies are needed to identify the exact mechanism by which carotenoids prevent lipid peroxidation and the amount needed for normal activity.

Source
Dixon ZR, et al. Effect of low carotene diet on malondialdehyde (MDA) concentration; Free Radic Biol Med. 1996.

Effect of consumption of tomato juice enriched with n-3 polyunsaturated fatty acids on the lipid profile, antioxidant biomarker status, and cardiovascular disease risk in healthy women

ABSTRACT
INTRODUCTION
Epidemiologic evidence suggests that tomato-based products could reduce the risk of cardiovascular diseases. One of the main cardiovascular risk factors is low levels of high-density lipoprotein cholesterol (HDL-C). This study aimed to prospectively evaluate the effect of tomato consumption on HDL-C levels.

SUBJECT AND METHODS
We conducted a randomized, single-blinded, controlled clinical trial. We screened 432 subjects with a complete lipid profile. Those individuals with low HDL-C (men <40 mg/dL and women <50 mg/dL) but normal triglyceride levels (<150 mg/dL) were included. Selected participants completed a 2-week run-in period on an isocaloric diet and then were randomized to receive 300 g of cucumber (control group) or two uncooked Roma tomatoes a day for 4 weeks.

RESULTS:
A total of 50 individuals (women = 41; 82%) with a mean age of 42 ± 15.5 years and a mean body mass index of 27.6 ± 5.0 kg/m2 completed the study. A significant increase in HDL-C levels was observed in the tomato group (from 36.5 ± 7.5 mg/dL to 41.6 ± 6.9 mg/dL, $P < 0.0001$ versus the control group). After stratification by gender, the difference in HDL-C levels was only significant in women. The mean HDL-C increase was 5.0 ± 2.8 mg/dL (range 1–12 mg/dL). Twenty patients (40%) finished the study with levels >40 mg/dL. A linear regression model that adjusted for those parameters that impact HDL-C levels (age, gender, waist-to-hip ratio, body mass index, fasting triglyceride concentration, simple sugars, alcohol, physical activity, and omega-3 consumption) showed an independent association between tomato consumption and the increase in HDL-C ($r^2 = 0.69$; $P < 0.0001$).

CONCLUSION:
Raw tomato consumption produced a favorable effect on HDL-C levels in overweight women.

Source
García-Alonso FJ, et al. Effect of consumption of tomato juice enriched with n-3 polyunsaturated fatty acids on the lipid profile, antioxidant biomarker status, and cardiovascular disease risk in healthy women. Eur J Nutr. 2012 Jun;51(4):415-24.

Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease

ABSTRACT
Most humans depend on sun exposure to satisfy their requirements for vitamin D. Solar ultraviolet B photons are absorbed by 7-dehydrocholesterol in the skin, leading to its transformation to previtamin D3, which is rapidly converted to vitamin D3. Season, latitude, time of day, skin pigmentation, aging, sunscreen use, and glass all influence the cutaneous production of vitamin D3. Once formed, vitamin D3 is metabolized in the liver to 25-hydroxyvitamin D3 and then in the kidney to its biologically active form, 1,25-dihydroxyvitamin D3. Vitamin D deficiency is an unrecognized epidemic among both children and adults in the United States. Vitamin D deficiency not only causes rickets among children but also precipitates and exacerbates osteoporosis among adults and causes the painful bone disease osteomalacia. Vitamin D deficiency has been associated with increased risks of deadly cancers, cardiovascular disease, multiple sclerosis, rheumatoid arthritis, and type 1 diabetes mellitus. Maintaining blood concentrations of 25-hydroxyvitamin D above 80 nmol/L (approximately 30 ng/mL) not only is important for maximizing intestinal calcium absorption but also may be important for providing the extrarenal 1alpha-hydroxylase that is present in most tissues to produce 1,25-dihydroxyvitamin D3. Although chronic excessive exposure to sunlight increases the risk of nonmelanoma skin cancer, the avoidance of all direct sun exposure increases the risk of vitamin D deficiency, which can have serious consequences. Monitoring serum 25-hydroxyvitamin D concentrations yearly should help reveal vitamin D deficiencies. Sensible sun exposure (usually 5-10 min of exposure of the arms and legs or the hands, arms, and face, 2 or 3 times per week) and increased dietary and supplemental vitamin D intakes are reasonable approaches to guarantee vitamin D sufficiency.

Source
Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr. 2004 Dec;80(6 Suppl):1678S-88S.

Vitamin C status and perception of effort during exercise in obese adults adhering to a calorie-reduced diet

ABSTRACT
OBJECTIVE:
Moderate energy restriction and exercise are recommended for effective weight

loss. Obese individuals oxidize less fat and report a higher perceived exertion during exercise, characteristics that may negatively influence exercise behavior. Because vitamin C status has been linked to fatigability, we compared the effects of vitamin C supplementation on self-reported fatigue and on the respiratory exchange ratio and the Ratings of Perceived Exertion scale during moderate exercise in healthy obese adults adhering to a hypocaloric diet.

METHODS:
Twenty adults (4 men and 16 women) were stratified and randomly assigned to receive 500 mg of vitamin C (VC) or placebo (CON) daily for 4 wk while adhering to a vitamin C-controlled, calorie-restricted diet. Feelings of general fatigue as assessed by the Profile of Mood States questionnaire were recorded on a separate day from the exercise session at weeks 0 and 4. Participants walked on a treadmill at an intensity of 50% predicted maximal oxygen consumption for 60 min at weeks 0 and 4, and heart rate, respiratory exchange ratio, and Ratings of Perceived Exertion were recorded.

RESULTS:
After 4 wk, the two groups lost similar amounts of weight (≈ 4 kg), and the respiratory exchange ratio was not altered by group. Heart rate and the Ratings of Perceived Exertion during exercise were significantly decreased in the VC versus the CON group (-11 versus -3 beats/min, P = 0.022, and -1.3 versus +0.1 U, P = 0.001, respectively), and the general fatigue score was decreased 5.9 U for the VC group versus a 1.9 U increase for the CON group (P = 0.001).

CONCLUSION:
These data provide preliminary evidence that vitamin C status may influence fatigue, heart rate, and perceptions of exertion during moderate exercise in obese individuals.

Source
Huck CJ et al. Vitamin C status and perception of effort during exercise in obese adults adhering to a calorie-reduced diet. Nutr [Epub June 5, 2012].

Docosapentaenoic acid (22:5n-3): a review of its biological effects.

ABSTRACT
This article summarizes the current knowledge available on metabolism and the biological effects of n-3 docosapentaenoic acid (DPA). n-3 DPA has not been extensively studied because of the limited availability of the pure compound. n-3 DPA is an elongated metabolite of EPA and is an intermediary product between EPA and DHA. The literature on n-3 DPA is limited, however the available data suggests it has beneficial health effects. In vitro n-3 DPA is retro-converted back to EPA, however it does not appear to be readily metabolised to DHA. In vivo studies have shown limited conversion of n-3 DPA to DHA, mainly in liver, but in addition retro-conversion to EPA is evident in a number of tissues. n-3 DPA can be metabolised by lipoxygenase, in platelets, to form ll-hydroxy-7,9,13,16,19- and 14-hydroxy-7,10,12,16,19-DPA. It has also been reported that n-3 DPA is effective (more so than EPA and DHA) in inhibition of aggregation in platelets obtained from rabbit blood. In addition, there is evidence that n-3 DPA possesses 10-fold greater endothelial cell migration ability than EPA, which is important in wound-healing processes. An in vivo study has reported that n-3 DPA reduces the fatty acid synthase and malic enzyme activity levels in n-3 DPA-supplemented mice and these effects were stronger than the EPA-supplemented mice. Another recent in vivo study has reported that n-3 DPA may have a role in attenuating age-related decrease in spatial learning and long-term potentiation. However, more research remains to be done to further investigate the biological effects of this n-3 VLCPUFA.

Source
Kaur G, et al. Docosapentaenoic acid (22:5n-3): a review of its biological effects. Progressive Lipid Research. 2011 Jan; 50(1):28-34

Effects of lycopene supplementation on oxidative stress and markers of endothelial function in healthy men

ABSTRACT
OBJECTIVE:
The objective was to determine the effects of lycopene supplementation on endothelial function assessed by reactive hyperemia peripheral arterial tonometry (RH-PAT) and oxidative stress.

Methods

Healthy men (n = 126) were randomized to receive placebo (n = 38), 6 mg (n = 41), or 15 mg (n = 37) lycopene daily for 8-week.

RESULTS:
Serum lycopene increased in a dose-dependent manner after 8-week supplementation (P < 0.001). The 15 mg/day group had greater increase in plasma SOD activity (P = 0.014) and reduction in lymphocyte DNA comet tail length (P = 0.042) than the placebo group. Intragroup comparison revealed a 23% increase in RH-PAT index from baseline (1.45 ± 0.09 vs. 1.79 ± 0.12; P = 0.032) in the 15 mg/day group after 8-week. hs-CRP, systolic blood pressure, sICAM-1 and sVCAM-1 significantly decreased, and β-carotene and LDL-particle size significantly increased only in the 15 mg/day group. Interestingly, the beneficial effect of lycopene supplementation on endothelial function (i.e., RH-PAT and sVCAM-1) were remarkable in subjects with relatively impaired endothelial cell function at initial level. Changes in RH-PAT index correlated with SOD activity (r = 0.234, P = 0.017) especially in the 15 mg lycopene/day group (r = 0.485, P = 0.003), lymphocyte DNA comet tail moment (r = –0.318, P = 0.001), and hs-CRP (r = –0.238, P = 0.011). In addition, changes in lycopene correlated with hs-CRP (r = –0.230, P = 0.016) and SOD activity (r = 0.205, P = 0.037).

CONCLUSION:
An increase in serum lycopene after supplementation can reduce oxidative stress which may play a role in endothelial function.

Source
Kim JY, et al. Effects of lycopene supplementation on oxidative stress and markers of endothelial function in healthy men. Atherosclerosis. 2011 Mar;215(1):189-95.

Omega-3 polyunsaturated fatty acids and cardiovascular diseases

ABSTRACT
Omega-3 polyunsaturated fatty acid (omega-3 PUFA) therapy continues to show great promise in primary and, particularly in secondary prevention of cardiovascular (CV) diseases. The most compelling evidence for CV benefits of omega-3 PUFA comes from 4 controlled trials of nearly 40,000 participants randomized to receive eicosapentaenoic acid (EPA) with or without docosahexaenoic acid (DHA) in studies of patients in primary prevention, after myocardial infarction, and most recently, with heart failure (HF). We discuss the evidence from retrospective epidemiologic studies and from large randomized controlled trials showing the benefits of omega-3 PUFA, specifically EPA and DHA, in primary and secondary CV prevention and provide insight into potential mechanisms of these observed benefits. The target EPA + DHA consumption should be at least 500 mg/day for individuals without underlying overt CV disease and at least 800 to 1,000 mg/day for individuals with known coronary heart disease and HF. Further studies are needed to determine optimal dosing and the relative ratio of DHA and EPA omega-3 PUFA that provides maximal cardioprotection in those at risk of CV disease as well in the treatment of atherosclerotic, arrhythmic, and primary myocardial disorders.

Source
Lavie CJ, et al. Omega-3 polyunsaturated fatty acids and cardiovascular diseases. J Am Coll Cardiol. 2009 Aug 11;54(7):585-94.

Prevention of sudden cardiac death by n-3 polyunsaturated fatty acids

ABSTRACT
There were already several epidemiologic studies that showed eating fish frequently seemed to reduce deaths from coronary heart disease. There were also observational and clinical trials that more specifically showed that the reduction in cardiovascular deaths from eating fish was largely the result of the prevention of sudden cardiac death by n-3 polyunsaturated fatty acids in fish oil. This led me to perform a clinical trial in which all subjects had an implanted cardioverter-defibrillator and were at very high risk of sudden cardiac death. The results of this study and the mechanisms by which n-3 fish oil fatty acids prevent fatal cardiac arrhythmias will be the subject of this review.

Source
Leaf A. Prevention of sudden cardiac death by n-3 polyunsaturated fatty acids. J Cardiovasc Med 2007; 8 Suppl 1:S27-29.

Fatty fish, marine omega-3 fatty acids and incidence of heart failure

ABSTRACT
BACKGROUND:
Marine omega-3 fatty acids have beneficial effects on cardiovascular risk factors. Consumption of fatty fish and marine omega-3 has been associated with lower rates of cardiovascular diseases.

OBJECTIVE:
We examined the association of fatty fish and marine omega-3 with heart failure (HF) in a population of middle-age and older women.

METHODS:
Participants in the Swedish Mammography Cohort aged 48–83 years completed 96-item food-frequency questionnaires. Women without history of HF, myocardial infarction, or diabetes at baseline (n= 36 234) were followed from January 1, 1998 until December 31, 2006 for HF hospitalization or mortality through Swedish inpatient and cause-of-death registers; 651 women experienced HF events. Cox proportional hazards models accounting for age and other confounders were used to calculate incidence rate ratios (RR) and 95% confidence intervals (CI).

RESULTS:
Compared to women who did not eat fatty fish, RR were 0.86 (95% CI: 0.67, 1.10) for <1 serving/week, 0.80 (95% CI: 0.63, 1.01) for 1 serving/week, 0.70 (95% CI: 0.53, 0.94) for 2 servings/week, and 0.91 (95% CI: 0.59, 1.40) for ≥3 servings/week (P_{trend} = 0.049). RR across quintiles of marine omega-3 fatty acids were 1 (reference), 0.85 (95% CI: 0.67, 1.07), 0.79 (95% CI: 0.61, 1.02), 0.83 (95% CI 0.65, 1.06), and 0.75 (95% CI: 0.58, 0.96) (P_{trend} = 0.04).

CONCLUSION:
Moderate consumption of fatty fish (one to two servings per week) and marine omega-3 fatty acids were associated with a lower rate of first HF hospitalization or death in this population.

Source
Levitan EB, et al. Fatty fish, marine omega-3 fatty acids and incidence of heart failure. eur J Clin Nutr. 2010 Jun;64(6):587-94. Epub 2010 Mar 24.

The omega-3 fatty acids EPA and DHA decrease plasma F(2)-isoprostanes: Results from two placebo-controlled interventions

ABSTRACT
Omega-3 (omega3) fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), protect against cardiovascular disease. Despite these benefits, concern remains that omega3 fatty acids may increase lipid peroxidation. It has previously been shown that urinary F(2)-isoprostanes (F(2)-IsoPs) were reduced following omega3 fatty acid supplementation

in humans. It is now determined whether EPA or DHA supplementation affects plasma F(2)-IsoPs. In two 6-week placebo-controlled interventions, Study A: overweight, dyslipidaemic men; and Study B: treated-hypertensive Type 2 diabetic, patients were randomized to 4 g daily EPA, DHA. Post-intervention plasma F(2)-IsoPs were significantly reduced by EPA (24% in Study A, 19% in Study B) and by DHA (14% in Study A, 23% in Study B) relative to the olive oil group. The fall in plasma F(2)-IsoPs was not altered in analyses that corrected for changes in plasma arachidonic acid, which was reduced with EPA and DHA supplementation. Neither F(3)- nor F(4)-IsoPs were observed in plasma in both studies. These results show that in humans, EPA and DHA reduce in vivo oxidant stress as measured in human plasma and urine.

Source
Mas E, et al. The omega-3 fatty acids EPA and DHA decrease plasma F(2)-isoprostanes: Results from two placebo-controlled interventions. Free Radic Res. 2010 Jun 14. [Epub ahead of print]

Oral magnesium supplementation in adults with coronary heart disease or coronary heart disease risk

ABSTRACT

PURPOSE:
To review randomized control clinical trial (RCT) literature and prospective studies for the safety and efficacy of magnesium supplements in patients with coronary heart disease (CHD) or with CHD risk.

DATA SOURCES:
Databases were searched using the keywords: magnesium, heart disease, endothelium, prevention, treatment, therapy, level, and supplement.

CONCLUSIONS:
There were no reports of adverse effects from magnesium supplementation in any of the studies. Subjects reporting lower dietary magnesium intake had significantly lower serum magnesium concentrations than those reporting higher dietary magnesium intake and, in some cases, had a significantly higher frequency of supraventricular beats. There was a modest relationship between dietary magnesium intake and a reduced risk of CHD in male subjects; however, there was no noted decrease in the development of CHD disease in women who had high magnesium intake.

IMPLICATIONS FOR PRACTICE:
Magnesium is vital for many functions in the body and magnesium supplementation is safe. There is a possible association between a modestly lower risk of CHD in men and increased magnesium intake; therefore, it is reasonable to encourage diets high in magnesium as a potential means to lower the risk of CHD.

Source
Mathers TW, et al. Oral magnesium supplementation in adults with coronary heart disease or coronary heart disease risk. J Am Acad Nurs Pract. 2009 Dec; 21(12):651-7

Serum 25-Hydroxyvitamin D Levels and the Prevalence of Peripheral Arterial Disease. Results from NHANES 2001 to 2004

ABSTRACT

OBJECTIVE:
The purpose of this study was to determine the association between 25-hydroxyvitamin D (25(OH)D) levels and the prevalence of peripheral arterial disease (PAD) in the general United States population.

METHODS AND RESULTS:
We analyzed data from 4839 participants of the National Health and Nutrition Examination Survey 2001 to 2004 to evaluate the relationship between 25(OH)D and PAD (defined as an ankle-brachial index < 0.9). Across quartiles of 25(OH)D, from lowest to highest, the prevalence of PAD was 8.1%, 5.4%, 4.9%, and 3.7% (P trend < 0.001). After multivariable adjustment for demographics, comorbidities, physical activity level, and laboratory measures, the prevalence ratio of PAD for the lowest, compared to the highest, 25(OH)D quartile (< 17.8 and > or = 29.2 ng/mL, respectively) was 1.80 (95% confidence interval: 1.19, 2.74). For each 10 ng/mL lower 25(OH)D level, the multivariable-adjusted prevalence ratio of PAD was 1.35 (95% confidence interval: 1.15, 1.59).

CONCLUSIONS:
Low serum 25(OH)D levels are associated with a higher prevalence of PAD. Several mechanisms have been invoked in the literature to support a potential antiatherosclerotic activity of vitamin D. Prospective cohort and mechanistic studies should be designed to confirm this association.

Source
Melamed ML, et al. Serum 25-Hydroxyvitamin D Levels and the Prevalence of Peripheral Arterial Disease. Results from NHANES 2001 to 2004. Arterioscler. Thromb. Vasc. Biol. 2008; 28 (6): 1179

Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial

ABSTRACT

BACKGROUND:
A suboptimal vitamin D and calcium status has been associated with higher risk of type 2 diabetes in observational studies, but evidence from trials is lacking.

OBJECTIVE:
We determined whether vitamin D supplementation, with or without calcium, improved glucose homeostasis in adults at high risk of diabetes.

DESIGN:
Ninety-two adults were randomly assigned in a 2-by-2 factorial-design, double-masked, placebo-controlled trial to receive either cholecalciferol (2000 IU once daily) or

calcium carbonate (400 mg twice daily) for 16 wk. The primary outcome was the change in pancreatic β cell function as measured by the disposition index after an intravenous-glucose-tolerance test. Other outcomes were acute insulin response, insulin sensitivity, and measures of glycemia.

RESULTS:
Participants had a mean age of 57 y, a body mass index (BMI; in kg/m(2)) of 32, and glycated hemoglobin (Hb A(1c)) of 5.9%. There was no significant vitamin D × calcium interaction on any outcomes. The disposition index increased in the vitamin D group and decreased in the no-vitamin D group (adjusted mean change ± SE: 300 ± 130 compared with -126 ± 127, respectively; P = 0.011), which was explained by an improvement in insulin secretion (62 ± 39 compared with -36 ± 37 mU · L(-1) · min, respectively; P = 0.046). Hb A(1c) increased less, but nonsignificantly, in the vitamin D group than in the no-vitamin D group (0.06 ± 0.03% compared with 0.14 ± 0.03%, respectively; P = 0.081). There was no significant difference in any outcomes with calcium compared with no calcium.

CONCLUSION:
In adults at risk of type 2 diabetes, short-term supplementation with cholecalciferol improved β cell function and had a marginal effect on attenuating the rise in Hb A(1c).

Source
Mitri J et al. Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. Am J

Circulating long-chain omega-3 fatty acids in incidence of congestive heart failure in older adults

ABSTRACT
BACKGROUND:
Few previous studies have evaluated associations between long-chain ω-3 fatty acids and incidence of congestive heart failure (CHF), and those that have are typically based on diet questionnaires and yield conflicting results. Circulating fatty acid concentrations provide objective biomarkers of exposure.

OBJECTIVE:
To determine whether plasma phospholipid concentrations of long-chain ω-3 fatty acids, including eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA), were associated with incident CHF.

DESIGN:
Prospective cohort study. Setting: 4 U.S. communities.

PATIENTS:
2735 U.S. adults without prevalent heart disease who were enrolled in the Cardiovascular Health Study from 1992 to 2006.

MEASUREMENTS:
Plasma phospholipid fatty acid concentrations and other cardiovascular risk factors were measured in 1992 by using standardized methods. Relationships with incident CHF (555 cases during 26 490 person-years, adjudicated by using medical records) were assessed by using Cox proportional hazards models.

RESULTS:
After multivariate adjustment, plasma phospholipid EPA concentration was inversely associated with incident CHF; risk was approximately 50% lower in the highest versus the lowest quartile (hazard ratio [HR], 0.52 [95% CI, 0.38 to 0.72]; P for trend = 0.001). In similar analyses, trends toward lower risk were seen for DPA (HR, 0.76 [CI, 0.56 to 1.04]; P for trend = 0.057) and total long-chain ω-3 fatty acids (HR, 0.70 [CI, 0.49 to 0.99]; P for trend = 0.062) but not for DHA (HR, 0.84 [CI, 0.58 to 1.21]; P for trend = 0.38). In analyses censored to the middle of follow-up (7 years) to minimize exposure misclassification over time, multivariate-adjusted HRs were 0.48 for EPA (CI, 0.32 to 0.71; P for trend = 0.005), 0.61 for DPA (CI, 0.39 to 0.95; P for trend = 0.033), 0.64 for DHA (CI, 0.40 to 1.04; P for trend = 0.057), and 0.51 for total ω-3 fatty acids (CI, 0.32 to 0.80; P for trend = 0.003).

LIMITATIONS:
Temporal changes in fatty acid concentrations over time may have caused underestimation of associations. Unmeasured or imperfectly measured covariates may have caused residual confounding.

CONCLUSION:
Circulating individual and total ω-3 fatty acid concentrations are associated with lower incidence of CHF in older adults.

Source
Mozaffarian D, et al. Circulating long-chain omega-3 fatty acids in incidence of congestive heart failure in older adults. Annals of Internal Medicine, 2011 August 2; 155(3):160-70

Relationship of serum and dietary magnesium to incident hypertension: the Atherosclerosis Risk in Communities (ARIC) Study

ABSTRACT
PURPOSE:
To examine the relationship of serum and dietary magnesium (Mg) with incident hypertension. The setting was the Atherosclerosis Risk in Communities (ARIC) Study, which included a biracial cohort, aged 45-64 years, from four U.S. communities.

METHODS:
This analysis included 7731 participants (4190 women and 3541 men) free of hypertension at baseline and followed six years. Fasting serum Mg was measured, and usual dietary intake was assessed with a food frequency questionnaire.

RESULTS:
After adjustment for age, race, and a number of other risk factors, the odds of incident hypertension across ascending quartiles of serum Mg were 1.0, 0.79, 0.85, and 0.70 in women (p trend = 0.01) and 1.0, 0.87, 0.87, and 0.82 in men (p trend = 0.16). We found no association between

dietary Mg intake and incident hypertension. These associations were attenuated after the addition of baseline systolic blood pressure to the models.

CONCLUSIONS:
This study suggests that low Mg may play a modest role in the development of hypertension.

Source
Peacock JM, et al. Relationship of serum and dietary magnesium to incident hypertension: the Atherosclerosis Risk in Communities (ARIC) Study. Annals of Epidemiology 1999;9:159-65.

Multivitamin use and the risk of myocardial infarction: a population-based cohort of Swedish women

ABSTRACT
BACKGROUND:
Dietary supplements are widely used in industrialized countries.

OBJECTIVE:
The objective was to examine the association between multivitamin use and myocardial infarction (MI) in a prospective, population-based cohort of women.

DESIGN:
The study included 31,671 women with no history of cardiovascular disease (CVD) and 2262 women with a history of CVD aged 49-83 y from Sweden. Women completed a self-administered questionnaire in 1997 regarding dietary supplement use, diet, and lifestyle factors. Multivitamins were estimated to contain nutrients close to recommended daily allowances: vitamin A (0.9 mg), vitamin C (60 mg), vitamin D (5 µg),vitamin E (9 mg), thiamine (1.2 mg), riboflavin (1.4 mg), vitamin B-6 (1.8 mg), vitamin B-12 (3 µg), and folic acid (400 µg).

RESULTS:
During an average of 10.2 y of follow-up, 932 MI cases were identified in the CVD-free group and 269 cases in the CVD group. In the CVD-free group, use of multivitamins only, compared with no use of supplements, was associated with a multivariable-adjusted hazard ratio (HR) of 0.73 (95% CI: 0.57, 0.93). The HR for multivitamin use together with other supplements was 0.70 (95% CI: 0.57, 0.87). The HR for use of supplements other than multivitamins was 0.93 (95% CI: 0.81, 1.08). The use of multivitamins for ≥5 y was associated with an HR of 0.59 (95% CI: 0.44, 0.80). In the CVD group, use of multivitamins alone or together with other supplements was not associated with MI.

CONCLUSIONS:
The use of multivitamins was inversely associated with MI, especially long-term use among women with no CVD. Further prospective studies with detailed information on the content of preparations and the duration of use are needed to confirm or refute our findings.

Source
Rautiainen S et al. Multivitamin use and the risk of myocardial infarction: a population-based cohort of Swedish women. Am J Clin Nutr. 95:1251-6, 2010.

Fish oil-derived fatty acids, docosahexaenoic acid and docosapentaenoic acid, and the risk of acute coronary events

ABSTRACT
BACKGROUND:
Previous findings concerning the serum levels of fish-derived (n-3) fatty acids and coronary heart disease are inconsistent. The purpose of this study was to investigate the association between the serum n-3 end-product fatty acids docosahexaenoic acid (DHA), docosapentaenoic acid (DPA), and eicosapentaenoic acid and the risk of acute coronary events in middle-aged men.

METHODS AND RESULTS:
We studied this association in the Kuopio Ischaemic Heart Disease Risk Factor Study, a prospective population study in Eastern Finland. Subjects were randomly selected and included 1871 men aged 42 to 60 years who had no clinical coronary heart disease at baseline examination. A total of 194 men had a fatal or nonfatal acute coronary event during follow-up. In a Cox proportional hazards' model adjusting for other risk factors, men in the highest fifth of the proportion of serum DHA+DPA in all fatty acids had a 44% reduced risk (P=0.014) of acute coronary events compared with men in the lowest fifth. Men in the highest fifth of DHA+DPA who had a low hair content of mercury (</=2.0 microgram/g) had a 67% reduced risk (P=0.016) of acute coronary events compared with men in the lowest fifth who had a high hair content of mercury (>2.0 microgram/g). There was no association between proportion of eicosapentaenoic acid and the risk of acute coronary events.

CONCLUSIONS:
Our data provide further confirmation for the concept that fish oil-derived fatty acids reduce the risk of acute coronary events. However, a high mercury content in fish could attenuate this protective effect.

Source
Rissanen T, et al. Fish oil-derived fatty acids, docosahexaenoic acid and docosapentaenoic acid, and the risk of acute coronary events. Circulation. 2000, Nov 28; 102(22): 2677-9

Calcium and vitamin D supplementation is associated with decreased abdominal visceral adipose tissue in overweight and obese adults

ABSTRACT
BACKGROUND:
Several studies suggest that calcium and vitamin D (CaD) may play a role in the regulation of abdominal fat mass.

OBJECTIVE:
This study investigated the effect of CaD-supplemented orange juice (OJ) on weight

loss and reduction of visceral adipose tissue (VAT) in overweight and obese adults (mean ± SD age: 40.0 ± 12.9 y).

DESIGN:
Two parallel, double-blind, placebo-controlled trials were conducted with either regular or reduced-energy (lite) orange juice. For each 16-wk trial, 171 participants were randomly assigned to 1 of 2 groups. The treatment groups consumed three 240-mL glasses of OJ (regular or lite) fortified with 350 mg Ca and 100 IU vitamin D per serving, and the control groups consumed either unfortified regular or lite OJ. Computed tomography scans of VAT and subcutaneous adipose tissue were performed by imaging a single cut at the lumbar 4 level.

RESULTS:
After 16 wk, the average weight loss (2.45 kg) did not differ significantly between groups. In the regular OJ trial, the reduction of VAT was significantly greater (P = 0.024) in the CaD group (-12.7 ± 25.0 cm(2)) than in the control group (-1.3 ± 13.6 cm(2)). In the lite OJ trial, the reduction of VAT was significantly greater (P = 0.039) in the CaD group (-13.1 ± 18.4 cm(2)) than in the control group (-6.4 ± 17.5 cm(2)) after control for baseline VAT. The effect of calcium and vitamin D on VAT remained highly significant when the results of the 2 trials were combined (P = 0.007).

CONCLUSIONS:
The findings suggest that calcium and/or vitamin D supplementation contributes to a beneficial reduction of VAT. This trial is registered at clinicaltrial.gov as NCT00386672, NCT01363115.

Source
Rosenblum JL et al. Calcium and vitamin D supplementation is associated with decreased abdominal visceral adipose tissue in overweight and obese adults. Am J Clin Nutr 95:101-8, 2011.

Magnesium. An update on physiological, clinical and analytical aspects

ABSTRACT
There is an increased interest in the role of magnesium ions in clinical medicine, nutrition and physiology. The characteristics of the binding of magnesium and calcium ions to various components, macromolecules and biological membranes are described. Magnesium affects many cellular functions, including transport of potassium and calcium ions, and modulates signal transduction, energy metabolism and cell proliferation. The mechanism of cellular uptake and efflux of magnesium, its intracellular transport, intestinal absorption, renal excretion and the effect of hormones on these are reviewed. Magnesium deficiency is not uncommon among the general population: its intake has decreased over the years especially in the western world. The magnesium supplementation or intravenous infusion may be beneficial in various diseased states. Of special interest is the magnesium status in alcoholism, eclampsia, hypertension, atherosclerosis, cardiac diseases, diabetes, and asthma. The development of instrumentation for the assay of ionized magnesium is reviewed, as are the analytical procedures for total magnesium in blood and free magnesium in the cytosol. The improved procedures for the assay of different magnesium states are useful in understanding the role of magnesium in health and disease.

Source
Saris NE, et al. Magnesium. An update on physiological, clinical and analytical aspects. Clin Chim Acta. 2000 Apr;294(1-2):1-26.

Savica V et al. The effect of nutrition on blood pressure. Annu Rev Nutr 30:365-401, 2010.

ABSTRACT
The incidence and severity of hypertension are affected by nutritional status and intake of many nutrients. Excessive energy intake and obesity are major causes of hypertension. Obesity is associated with increased activity of the renin-angiotensin-aldosterone and sympathetic nervous systems, possibly other mineralcorticoid activity, insulin resistance, salt-sensitive hypertension and excess salt intake, and reduced kidney function. High sodium chloride intake strongly predisposes to hypertension. Increased alcohol consumption may acutely elevate blood pressure. High intakes of potassium, polyunsaturated fatty acids, and protein, along with exercise and possibly vitamin D, may reduce blood pressure. Less-conclusive studies suggest that amino acids, tea, green coffee bean extract, dark chocolate, and foods high in nitrates may reduce blood pressure. Short-term studies indicate that specialized diets may prevent or ameliorate mild hypertension; most notable are the Dietary Approaches to Stop Hypertension (DASH) diet, which is high in fruits, vegetables, and low-fat dairy products, and the DASH low-sodium diet. Long-term compliance to these diets remains a major concern.

Source
Savica V et al. The effect of nutrition on blood pressure. Annu Rev Nutr 30:365-401, 2010.

Greater Whole-Grain Intake Is Associated with Lower Risk of Type 2 Diabetes, Cardiovascular Disease, and Weight Gain

ABSTRACT
Whole-grain and high fiber intakes are routinely recommended for prevention of vascular diseases; however, there are no comprehensive and quantitative assessments of available data in humans. The aim of this study was to systematically examine longitudinal studies investigating whole-grain and fiber intake in relation to risk of type 2 diabetes (T2D), cardiovascular disease (CVD), weight gain, and metabolic risk factors. We identified 45 prospective cohort studies and

21 randomized-controlled trials (RCT) between 1966 and February 2012 by searching the Cumulative Index to Nursing and Allied Health Literature, Cochrane, Elsevier Medical Database, and PubMed. Study characteristics, whole-grain and dietary fiber intakes, and risk estimates were extracted using a standardized protocol. Using random effects models, we found that compared with never/rare consumers of whole grains, those consuming 48-80 g whole grain/d (3-5 serving/d) had an ~26% lower risk of T2D [RR = 0.74 (95% CI: 0.69, 0.80)], ~21% lower risk of CVD [RR = 0.79 (95% CI: 0.74, 0.85)], and consistently less weight gain during 8-13 y (1.27 vs 1.64 kg; P = 0.001). Among RCT, weighted mean differences in post-intervention circulating concentrations of fasting glucose and total and LDL-cholesterol comparing whole-grain intervention groups with controls indicated significantly lower concentrations after whole-grain interventions [differences in fasting glucose: -0.93 mmol/L (95% CI: -1.65, -0.21), total cholesterol: -0.83 mmol/L (-1.23, -0.42); and LDL-cholesterol: -0.82 mmol/L (-1.31, -0.33)]. [corrected] Findings from this meta-analysis provide evidence to support beneficial effects of whole-grain intake on vascular disease prevention. Potential mechanisms responsible for whole grains' effects on metabolic intermediates require further investigation in large intervention trials.

Source
Ye EQ et al. Greater Whole-Grain Intake Is Associated with Lower Risk of Type 2 Diabetes, Cardiovascular Disease, and Weight Gain. J Nutr 142:1304-13, July, 2012 Epub May 30, 2012].

IMMUNE HEALTH

Recent advances in clinical research involving carotenoids

ABSTRACT
Epidemiological studies show consistent decreased risk of lung cancer and certain other cancers, cataracts, age-related macular degeneration, and coronary heart disease in populations with the highest intakes of carotenoid-rich diets. Intervention studies show reductions in precancerous oral lesions, enhancement in immune parameters, and reduced incidence of cardiovascular events in individuals supplemented with β-carotene.

Source
Bendich A, et al. Recent advances in clinical research involving carotenoids. Pure & Appl Chem. 1994;66(5): 1017-1024.

Physicians and nurses use and recommend dietary supplements: report of a survey

ABSTRACT
BACKGROUND:
Numerous surveys show that dietary supplements are used by a large proportion of the general public, but there have been relatively few surveys on the prevalence of dietary supplement use among health professionals, including physicians and nurses. Even less information is available regarding the extent to which physicians and nurses recommend dietary supplements to their patients.

METHODS:
An online survey was administered in October 2007 to 900 physicians and 277 nurses by Ipsos Public Affairs for the Council for Responsible Nutrition (CRN), a trade association representing the dietary supplement industry. The health professionals were asked whether they used dietary supplements and their reasons for doing so, and whether they recommend dietary supplements to their patients.

RESULTS:
The "Life...supplemented" Healthcare Professionals Impact Study (HCP Impact Study) found that 72% of physicians and 89% of nurses in this sample used dietary supplements regularly, occasionally, or seasonally. Regular use of dietary supplements was reported by 51% of physicians and 59% of nurses. The most common reason given for using dietary supplements was for overall health and wellness (40% of physicians and 48% of nurses), but more than two-thirds cited more than one reason for using the products. When asked whether they "ever recommend dietary supplements" to their patients, 79% of physicians and 82% of nurses said they did.

CONCLUSION:
Physicians and nurses are as likely as members of the general public to use dietary supplements, as shown by comparing the results of this survey with data from national health and nutrition surveys. Also, most physicians and nurses recommend supplements to their patients, whether or not the clinicians use dietary supplements themselves.

Source
Dickinson A, et al. Physicians and nurses use and recommend dietary supplements: report of a survey. Nutr J. 2009 Jul 1;8:29.

Effects of a carotene-deficient diet on measures of oxidative susceptibility and superoxide dismutase activity in adult women

ABSTRACT
The effect of consuming a low carotene diet (approximately 60 micrograms carotene/day) on oxidative susceptibility and superoxide dismutase (SOD) activity in women living in a metabolic research unit was evaluated. The diet had sufficient vitamins A, E, and C. The women ate the diet supplemented with 1500 micrograms/day beta-carotene for 4 days (baseline), then the unsupplemented diet for 68 days (depletion), followed by the diet supplemented with > 15,000 micrograms/day carotene for 28 days (repletion). Production of hexanal, pentanal, and pentane by copper-oxidized plasma low density lipoproteins from carotene-depleted women was greater than their production of these compounds when repleted with carotene. Erythrocyte SOD activity was depressed in

carotene-depleted women; it recovered with repletion. Thiobarbituric acid reactive substances in plasma of carotene-depleted women were elevated and diminished with repletion. Dietary carotene seems to be needed, not only as a precursor of vitamin A, but also to inhibit oxidative damage and decrease oxidation susceptibility.

Source
Dixon ZR, et al. Effects of a carotene-deficient diet on measures of oxidative susceptibility and superoxide dismutase activity in adult women. Free Radic Biol Med. 1994 Dec;17(6):537-44.

Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial

ABSTRACT

BACKGROUND:
A suboptimal vitamin D and calcium status has been associated with higher risk of type 2 diabetes in observational studies, but evidence from trials is lacking.

OBJECTIVE:
We determined whether vitamin D supplementation, with or without calcium, improved glucose homeostasis in adults at high risk of diabetes.

DESIGN:
Ninety-two adults were randomly assigned in a 2-by-2 factorial-design, double-masked, placebo-controlled trial to receive either cholecalciferol (2000 IU once daily) or calcium carbonate (400 mg twice daily) for 16 wk. The primary outcome was the change in pancreatic β cell function as measured by the disposition index after an intravenous-glucose-tolerance test. Other outcomes were acute insulin response, insulin sensitivity, and measures of glycemia.

RESULTS:
Participants had a mean age of 57 y, a body mass index (BMI; in kg/m(2)) of 32, and glycated hemoglobin (Hb A(1c)) of 5.9%. There was no significant vitamin D × calcium interaction on any outcomes. The disposition index increased in the vitamin D group and decreased in the no-vitamin D group (adjusted mean change ± SE: 300 ± 130 compared with -126 ± 127, respectively; P = 0.011), which was explained by an improvement in insulin secretion (62 ± 39 compared with -36 ± 37 mU · L(-1) · min, respectively; P = 0.046). Hb A(1c) increased less, but nonsignificantly, in the vitamin D group than in the no-vitamin D group (0.06 ± 0.03% compared with 0.14 ± 0.03%, respectively; P = 0.081). There was no significant difference in any outcomes with calcium compared with no calcium.

CONCLUSION:
In adults at risk of type 2 diabetes, short-term supplementation with cholecalciferol improved β cell function and had a marginal effect on attenuating the rise in Hb A(1c).

Source
Mitri J et al. Effects of vitamin D and calcium supplementation on pancreatic B cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. Am J

Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis

ABSTRACT

CONTEXT:
Epidemiological and experimental evidence suggests that high levels of vitamin D, a potent immunomodulator, may decrease the risk of multiple sclerosis. There are no prospective studies addressing this hypothesis.

OBJECTIVE:
To examine whether levels of 25-hydroxyvitamin D are associated with risk of multiple sclerosis.

DESIGN, SETTING, AND PARTICIPANTS:
Prospective, nested case-control study among more than 7 million US military personnel who have serum samples stored in the Department of Defense Serum Repository. Multiple sclerosis cases were identified through Army and Navy physical disability databases for 1992 through 2004, and diagnoses were confirmed by medical record review. Each case (n = 257) was matched to 2 controls by age, sex, race/ethnicity, and dates of blood collection. Vitamin D status was estimated by averaging 25-hydroxyvitamin D levels of 2 or more serum samples collected before the date of initial multiple sclerosis symptoms.

MAIN OUTCOME MEASURES:
Odds ratios of multiple sclerosis associated with continuous or categorical levels (quantiles or a priori-defined categories) of serum 25-hydroxyvitamin D within each racial/ethnic group.

RESULTS:
Among whites (148 cases, 296 controls), the risk of multiple sclerosis significantly decreased with increasing levels of 25-hydroxyvitamin D (odds ratio [OR] for a 50-nmol/L increase in 25-hydroxyvitamin D, 0.59; 95% confidence interval, 0.36-0.97). In categorical analyses using the lowest quintile (<63.3 nmol/L) as the reference, the ORs for each subsequent quintile were 0.57, 0.57, 0.74, and 0.38 (P = .02 for trend across quintiles). Only the OR for the highest quintile, corresponding to 25-hydroxyvitamin D levels higher than 99.1 nmol/L, was significantly different from 1.00 (OR, 0.38; 95% confidence interval, 0.19-0.75; P = .006). The inverse relation with multiple sclerosis risk was particularly strong for 25-hydroxyvitamin D levels measured before age 20 years. Among blacks and Hispanics (109 cases, 218 controls), who had lower 25-hydroxyvitamin D levels than whites, no significant associations between vitamin D and multiple sclerosis risk were found.

CONCLUSION:
The results of our study suggest that high circulating levels of vitamin D are associated with a lower risk of multiple sclerosis.

Source
Munger KL , et al. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA. 2006 Dec 20;296(23):2832-8.

Vitamin D controls T cell antigen receptor signaling and activation of human T cells

ABSTRACT
Phospholipase C (PLC) isozymes are key signaling proteins downstream of many extracellular stimuli. Here we show that naive human T cells had very low expression of PLC-gamma1 and that this correlated with low T cell antigen receptor (TCR) responsiveness in naive T cells. However, TCR triggering led to an upregulation of approximately 75-fold in PLC-gamma1 expression, which correlated with greater TCR responsiveness. Induction of PLC-gamma1 was dependent on vitamin D and expression of the vitamin D receptor (VDR). Naive T cells did not express VDR, but VDR expression was induced by TCR signaling via the alternative mitogen-activated protein kinase p38 pathway. Thus, initial TCR signaling via p38 leads to successive induction of VDR and PLC-gamma1, which are required for subsequent classical TCR signaling and T cell activation.

Source
von Essen MR, et al. Vitamin D controls T cell antigen receptor signaling and activation of human T cells. Nat Immunol. 2010 Apr;11(4):344-9.

Update: effects of antioxidant and non-antioxidant vitamin supplementation on immune function

ABSTRACT
The purpose of this manuscript is to review the impact of supplementation with vitamins E and C, carotenoids, and the B vitamins on parameters of innate and adaptive immune function as reported from clinical trials in humans. There is evidence to support causal effects of supplementation with vitamins E and C and the carotenoids singly and in combination on selected aspects of immunity, including the functional capacity of innate immune cells, lymphocyte proliferation, and the delayed-type hypersensitivity (DTH) response. Controlled intervention trials of B vitamin-containing multivitamin supplements suggest beneficial effects on immune parameters and clinical outcomes in HIV-positive individuals.

Source
Webb AL, et al. Update: effects of antioxidant and non-antioxidant vitamin supplementation on immune function. Nutr Rev. 2007 May;65(5):181-217.

LUNG HEALTH

The omega-3 fatty acids EPA and DHA decrease plasma F(2)-isoprostanes: Results from two placebo-controlled interventions

ABSTRACT
Omega-3 (omega3) fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), protect against cardiovascular disease. Despite these benefits, concern remains that omega3 fatty acids may increase lipid peroxidation. It has previously been shown that urinary F(2)-isoprostanes (F(2)-IsoPs) were reduced following omega3 fatty acid supplementation in humans. It is now determined whether EPA or DHA supplementation affects plasma F(2)-IsoPs. In two 6-week placebo-controlled interventions, Study A: overweight, dyslipidaemic men; and Study B: treated-hypertensive Type 2 diabetic, patients were randomized to 4 g daily EPA, DHA. Post-intervention plasma F(2)-IsoPs were significantly reduced by EPA (24% in Study A, 19% in Study B) and by DHA (14% in Study A, 23% in Study B) relative to the olive oil group. The fall in plasma F(2)-IsoPs was not altered in analyses that corrected for changes in plasma arachidonic acid, which was reduced with EPA and DHA supplementation. Neither F(3)- nor F(4)-IsoPs were observed in plasma in both studies. These results show that in humans, EPA and DHA reduce in vivo oxidant stress as measured in human plasma and urine.

Source
Mas E, et al. The omega-3 fatty acids EPA and DHA decrease plasma F(2)-isoprostanes: Results from two placebo-controlled interventions. Free Radic Res. 2010 Jun 14. [Epub ahead of print]

Intake of specific carotenoids and risk of lung cancer in 2 prospective US cohorts

ABSTRACT
BACKGROUND:
Carotenoids may reduce lung carcinogenesis because of their antioxidant properties; however, few studies have examined the relation between intakes of individual carotenoids and lung cancer risk.

OBJECTIVE:
The aim of this study was to examine the relation between lung cancer risk and intakes of alpha-carotene, beta-carotene, lutein, lycopene, and beta-cryptoxanthin in 2 large cohorts.

DESIGN:
During a 10-y follow-up period, 275 new cases of lung cancer were diagnosed in 46924 men; during a 12-y follow-up period, 519 new cases were diagnosed in 77283 women. Carotenoid intakes were derived from the reported consumption of fruit and vegetables on food-frequency questionnaires administered at baseline and during follow-up. The data were analyzed separately for each cohort and the results were pooled to compute overall relative risks (RRs).

RESULTS:
In the pooled analyses, alpha-carotene and lycopene intakes were significantly associated with a lower risk of lung cancer; the

association with beta-carotene, lutein, and beta-cryptoxanthin intakes were inverse but not significant. Lung cancer risk was significantly lower in subjects who consumed a diet high in a variety of carotenoids (RR: 0.68; 95% CI: 0.49, 0.94 for highest compared with lowest total carotenoid score category). Inverse associations were strongest after a 4-8-y lag between dietary assessment and date of diagnosis. In subjects who never smoked, a 63% lower incidence of lung cancer was observed for the top compared with the bottom quintile of alpha-carotene intake (RR: 0.37; 95% CI: 0.18, 0.77).

CONCLUSION:
Data from 2 cohort studies suggest that several carotenoids may reduce the risk of lung cancer.

Source
Michaud DS, et al. Intake of specific carotenoids and risk of lung cancer in 2 prospective US cohorts. Am J Clin Nutr. 2000 Oct;72(4):990-7.

The effects of omega-3 supplementation on pulmonary function of young wrestlers during intensive training

ABSTRACT
The purpose of this study was to examine the effects of omega-3 supplementation on young wrestler's pulmonary function during intensive wrestling training. Forty healthy young male wrestlers participated in this study. The subjects were randomly divided into experimental (n=10), placebo (n=10), active control (n=10) and inactive control (n=10) groups. Participants in experimental, placebo and active control groups performed wrestling incremental training up to 95% of exercise MHR, three times a week, for 12 weeks. The inactive control group did not participate in any exercisetraining. Subjects in the experimental group were asked to consume omega-3 (1000 mg/day for 12 weeks), while those in placebo were refused any doses of omega-3. The pulmonary variables were measured at baseline and at the end of 12 weeks of training program. Results indicated that consuming omega-3 during 12 weeks training had a significantly positive effect on pulmonary variables such as FEV1, FVC, VC, MVV, FEF25-75, FIV1 (p=0.001), but no significant changes were observed in FEV1% (p=0.141) and FIV1% (p=0.117). The results of the present study suggest that consuming omega-3 during intensive wrestling training can improve pulmonary function of athletes during and in post-exercise.

Source
Tartibian B, et al. The effects of omega-3 supplementation on pulmonary function of young wrestlers during intensive training. J Sci Med Sport. 2010 Mar;13(2):281-6.

MEN'S HEALTH

Attaman JA et al. Dietary fat and semen quality among men attending a fertility clinic. Hum Reprod 27:1466-74, 2012.

ABSTRACT
BACKGROUND:
The objective of this study was to examine the relation between dietary fats and semen quality parameters.

METHODS:
Data from 99 men with complete dietary and semen quality data were analyzed. Fatty acid levels in sperm and seminal plasma were measured using gas chromatography in a subgroup of men (n = 23). Linear regression was used to determine associations while adjusting for potential confounders.

RESULTS:
Men were primarily Caucasian (89%) with a mean (SD) age of 36.4 (5.3) years; 71% were overweight or obese; and 67% were never smokers. Higher total fat intake was negatively related to total sperm count and concentration. Men in the highest third of total fat intake had 43% (95% confidence interval (CI): 62–14%) lower total sperm count and 38% (95% CI: 58–10%) lower sperm concentration than men in the lowest third (P_{trend} = 0.01). This association was driven by intake of saturated fats. Levels of saturated fatty acids in sperm were also negatively related to sperm concentration (r= –0.53), but saturated fat intake was unrelated to sperm levels (r = 0.09). Higher intake of omega-3 polyunsaturated fats was related to a more favorable sperm morphology. Men in the highest third of omega-3 fatty acids had 1.9% (0.4–3.5%) higher normal morphology than men in the lowest third (P_{trend} = 0.02).

CONCLUSIONS:
In this preliminary cross-sectional study, high intake of saturated fats was negatively related to sperm concentration whereas higher intake of omega-3 fats was positively related to sperm morphology. Further, studies with larger samples are now required to confirm these findings.

Source
Attaman JA et al. Dietary fat and semen quality among men attending a fertility clinic. Hum Reprod 27:1466-74, 2012.

Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males

ABSTRACT
RATIONALE:
A significant proportion of the general population report supplementing their diet with one or more vitamins or minerals, with common reasons for doing so being to combat stress and fatigue and to improve mental functioning. Few studies have assessed the relationship between supplementation with vitamins/minerals and psychological functioning in healthy cohorts of non-elderly adults.

OBJECTIVES:
The present randomised, placebo-con-

trolled, double–blind, parallel groups trial assessed the cognitive and mood effects of a high-dose B-complex vitamin and mineral supplement (Berocca®) in 215 males aged 30 to 55 years, who were in full-time employment.

METHODS:
Participants attended the laboratory prior to and on the last day of a 33-day treatment period where they completed the Profile of Mood States (POMS), Perceived Stress Scale (PSS) and General Health Questionnaire (GHQ-12). Cognitive performance and task-related modulation of mood/fatigue were assessed with the 60 min cognitive demand battery. On the final day, participants also completed the Stroop task for 40 min whilst engaged in inclined treadmill walking and subsequent executive function was assessed.

Results:
Vitamin/mineral supplementation led to significant improvements in ratings on the PSS, GHQ-12 and the 'vigour' subscale of the POMS. The vitamin/mineral group also performed better on the Serial 3s subtractions task and rated themselves as less 'mentally tired' both pre- and post-completion of the cognitive demand battery.

Conclusions:
Healthy members of the general population may benefit from augmented levels of vitamins/minerals via direct dietary supplementation. Specifically, supplementation led to improved ratings of stress, mental health and vigour and improved cognitive performance during intense mental processing.

Source
Kennedy DO et al. Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. Psychopharmacol 211:55-68, 2010.

The association of folate, zinc and antioxidant intake with sperm aneuploidy in healthy non-smoking men

ABSTRACT
BACKGROUND:
Little is known about the effect of paternal nutrition on aneuploidy in sperm. We investigated the association of normal dietary and supplement intake of folate, zinc and antioxidants (vitamin C, vitamin E and beta-carotene) with the frequency of aneuploidy in human sperm.

METHODS:

Sperm samples from 89 healthy, non-smoking men from a non-clinical setting were analysed for aneuploidy using fluorescent in situ hybridization with probes for chromosomes X, Y and 21. Daily total intake (diet and supplements) for zinc, folate, vitamin C, vitamin E and beta-carotene was derived from a food frequency questionnaire. Potential confounders were obtained from a self-administered questionnaire.

RESULTS:
After adjusting for covariates, men with high folate intake (>75th percentile) had lower frequencies of sperm with disomies X, 21, sex nullisomy, and a lower aggregate measure of sperm aneuploidy (P <or= 0.04) compared with men with lower intake. In adjusted continuous analyses, total folate intake was inversely associated with aggregate sperm aneuploidy (-3.6% change/100 microg folate; 95% CI: -6.3, -0. 8) and results were similar for disomies X, 21 and sex nullisomy. No consistent associations were found between antioxidant or zinc intakes and sperm aneuploidy.

CONCLUSIONS:
Men with high folate intake had lower overall frequencies of several types of aneuploid sperm.

Source
Young SS, et al. The association of folate, zinc and antioxidant intake with sperm aneuploidy in healthy non-smoking men. Human Reprod Epub Mar 19, 2008.

OVARIAN HEALTH

The role of vitamin D in cancer prevention

ABSTRACT
Vitamin D status differs by latitude and race, with residents of the northeastern United States and individuals with more skin pigmentation being at increased risk of deficiency. A PubMed database search yielded 63 observational studies of vitamin D status in relation to cancer risk, including 30 of colon, 13 of breast, 26 of prostate, and 7 of ovarian cancer, and several that assessed the association of vitamin D receptor genotype with cancer risk. The majority of studies found a protective relationship between sufficient vitamin D status and lower risk of cancer. The evidence suggests that efforts to improve vitamin D status, for example by vitamin D supplementation, could reduce cancer incidence and mortality at low cost, with few or no adverse effects.

Source
Garland CF, et al. The role of vitamin D in cancer prevention. Am J Public Health. 2006 Feb;96(2):252-61.

Dietary carotenoids and risk of breast cancer in Chinese women

ABSTRACT
There has been considerable interest in the role of carotenoids in the chemoprevention of cancer. However, the protective effect of carotenoids on breast cancer has been inconclusive. To investigate whether intake of lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin is inversely associated with breast cancer risk, a case-control study was conducted in China during 2004-2005. The cases were 122 female patients aged 24-87 years with histopathologically confirmed breast cancer. 632 healthy women age-matched were randomly recruited from outpatient clinics. Habitual dietary intake and lifestyle were collected by face-to-face interview using a validated and reliable food frequency questionnaire. The USDA nutrient composition database was used to calculate intake of the specific carotenoids. Unconditional logistic regression analyses were used to

estimate odds ratios (ORs) and 95% confidence intervals (CIs), accounting for age, locality, education, body mass index, smoking, passive smoking, physical activity, number of children breastfed, menopausal status, oral contraceptive use, biopsy-confirmed benign breast diseases, family history of breast cancer, and total energy intake. Compared with the highest versus lowest quartile of intake, the adjusted ORs were 0.26 (95% CI 0.14-0.46) for lycopene, 0.38 (95% CI 0.21-0.71) for beta-carotene, 0.43 (95% CI 0.23-0.82) for beta-cryptoxanthin, and 0.37 (95% CI 0.20-0.68) for total carotenoids, with statistically significant tests for trend. There was no association with breast cancer for alpha-carotene and lutein/zeaxanthin. It is concluded that higher intake of lycopene, beta-carotene and beta-cryptoxanthin is associated to a lower risk of breast cancer among Chinese women. More research to examine the relationship between carotenoids and breast cancer risk is warranted.

Source
Huang JP, et al. Dietary carotenoids and risk of breast cancer in Chinese women. Asia Pac J Clin Nutr. 2007;16 Suppl 1:437-42.

Intake of specific carotenoids and the risk of epithelial ovarian cancer

ABSTRACT
There has been considerable interest in the role of carotenoids in the chemoprevention of cancer. However, few studies have examined the association between intake of specific carotenoids and the risk of epithelial ovarian cancer and the results for carotenoids have been inconclusive. To investigate whether the intake of alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein and zeaxanthin, and lycopene is inversely associated with ovarian cancer risk, a case-control study was conducted in China during 1999-2000. The cases were 254 patients with histologically confirmed epithelial ovarian cancer and 652 age-matched controls were randomly recruited during the same period. Habitual dietary intake and lifestyle were collected by face-to-face interview using a validated and reliable FFQ. The US Department of Agriculture nutrient composition database was used to calculate the intake of specific carotenoids. Unconditional logistic regression analyses were used to estimate OR and 95 % CI, accounting for age, locality, education, BMI, smoking, tea drinking, parity, oral contraceptive use, hormone replacement therapy, menopausal status, family history of ovarian cancer, physical activity and energy intake. Compared with the highest v. the lowest quartile of intake, the adjusted OR were 0.39 (95 % CI 0.23, 0.66) for alpha-carotene, 0.51 (95 % CI 0.31, 0.84) for beta-carotene, 0.51 (95 % CI 0.31, 0.83) for beta-cryptoxanthin, 0.45 (0.27, 0.76) for lutein and zeaxanthin, and 0.33 (95 % CI 0.20, 0.56) for total carotenoids, with statistically significant tests for trend. It is concluded that a higher intake of carotenoids can reduce the risk of epithelial ovarian cancer.

Source
Zhang M, et al. Intake of specific carotenoids and the risk of epithelial ovarian cancer. Br J Nutr. 2007 Jul;98(1):187-93. Epub 2007 Mar 19.

PROSTATE HEALTH

The promiscuous receptor

ABSTRACT
OBJECTIVE:
To determine the effectiveness of vitamin D therapy in patients with asymptomatic, prostate-specific antigen (PSA)-progression of prostate cancer.

PATIENTS AND METHODS:
Twenty-six patients with locally advanced or metastatic prostate cancer were treated with vitamin D. Vitamin D therapy was discontinued on disease progression as assessed by symptoms or serum PSA increase. The response to therapy was judged from changes in PSA level from the pretreatment baseline to 3 months after starting vitamin D therapy.

RESULTS:
Of the 26 patients, five (20%) responded to vitamin D; the mean (range) reduction in PSA level was 45.3 (15.9-95.1)%, and mean duration of response was 4-5 months. Patients in whom the PSA level was stabilized, but not reduced, after vitamin D treatment had a duration of response of up to 36 months. Treatment was well tolerated and was not associated with elevation of serum calcium levels. There was no significant correlation between response to therapy and stage of disease, Gleason grade, previous treatments or PSA level at diagnosis or initiation of vitamin D therapy.

CONCLUSION:
Vitamin D therapy is an effective and well tolerated treatment for patients with asymptomatic progressive prostate cancer, and is a useful addition to the therapeutic options.

Source
Newsom-Davis TE, et al. The promiscuous receptor. BJU Int. 2009 Nov;104(9):1204-7

Carotenoids and prostate cancer risk.

ABSTRACT
Chemoprevention is presumably one of most effective means to combat prostate cancer (PCa). Patients usually require more than a decade to develop a clinically significant Pca, therefore, an ideal target for chemoprevention. This review will focus on recent findings of a group of naturally occurring chemicals, carotenoids, for potential use in reducing PCa risk.

Source
Young CY, et al. Carotenoids and prostate cancer risk. Mini Rev Med Chem. 2008 May;8(5):529-37.

SKIN HEALTH

Dietary carotenoids contribute to normal human skin color and UV photosensitivity

ABSTRACT
The aim of the current study was to determine whether dietary carotenoids influence skin pigmentation and UV photosensitivity in a healthy unsupplemented panel (n = 22) of Caucasian (skin Type II) subjects. Skin spectrophotometric and tristimulus (L*a*b*) CR200 chromameter readings were made at various body sites to objectively measure skin carotenoid levels and skin color, respectively. The minimal erythemal dose (MED) was also measured to determine the intrinsic UV photosensitivity of the skin. We found that tristimulus b* values (but not L* and a* values) were consistently and closely correlated with skin carotenoid levels at a number of body sites including the back ($r = 0.85$, $P < 0.00001$), forehead ($r = 0.85$, $P < 0.00001$), inner forearm ($r = 0.75$, $P < 0.0001$) and palm of the hand ($r = 0.78$, $P < 0.0001$). Skin carotenoid levels and MED were also correlated in these subjects ($r = 0.66$, $P < 0.001$), as were tristimulus b* values and MED ($r = 0.71$, $P< 0.0002$). From these observations, we conclude that carotenoids from a normal, unsupplemented diet accumulate in the skin and confer a measurable photoprotective benefit (at least in lightly pigmented Caucasian skin), that is directly linked to their concentration in the tissue. Carotenoids also appear to contribute measurably and significantly to normal human skin color, in particular the appearance of "yellowness" as defined objectively by CR200 tristimulus b* values. On the basis of these findings we believe that objective measurements of skin color, in particular tristimulus b* values, may be a potentially useful means of monitoring dietary carotenoid status and assessing UV photosensitivity in Caucasian populations.

Source
Alaluf S, et al. Dietary carotenoids contribute to normal human skin color and UV photosensitivity. J Nutr 132: 399-403, 2002.

Oleic acid modulation of the immune response in wound healing: A new approach for skin repair

ABSTRACT
Injury triggers inflammatory responses and tissue repair. Several treatments are currently in use to accelerate healing; however, more efficient formulations are still needed for specific injuries. Since unsaturated fatty acids modulate immune responses, we aimed to evaluate their therapeutic effects on wound healing. Skin wounds were induced in BALB/c mice and treated for 5 days with n-3, n-9 fatty acids or vehicle (control). n-9 treated mice presented smaller wounds than control and n-3 at 120 h post-surgery (p.s.). Collagen III mRNA, TIMP1 and MMP9 were significantly elevated in n-9 group compared to n-3 or vehicle at 120 h p.s. Among the inflammatory mediators studied we found that IL-10, TNF-α and IL-17 were also higher in n-9 treated group compared to n-3 or vehicle at 120 h p.s. Interestingly, COX2 had decreased expression on wound tissue treated with n-9. Inflammatory infiltrate analysis revealed diminished frequency of CD4(+), CD8(+) and CD11b(+) cells in n-9 wounds at 24 and 120 h p.s., which was not related to cell death, since in vitro apoptosis experiments did not show any cell damage after fatty acids administration. These results suggested that unsaturated fatty acids, specifically n-9, modulate the inflammation in the wound and enhance reparative response in vivo. n-9 may be a useful tool in the treatment of cutaneous wounds.

Source
Cardoso CR, et al. Oleic acid modulation of the immune response in wound healing: A new approach for skin repair.
Immunobiology. 2010 Jul 22. [Epub ahead of print]

Dietary nutrient intakes and skin-aging appearance among middle-aged American women

ABSTRACT
BACKGROUND:
Nutritional factors play a key role in normal dermatologic functioning. However, little is known about the effects of diet on skin-aging appearance.

OBJECTIVE:
We evaluated the associations between nutrient intakes and skin-aging appearance.

DESIGN:
Using data from the first National Health and Nutrition Examination Survey, we examined associations between nutrient intakes and skin aging in 4025 women (40–74 y). Nutrients were estimated from a 24-h recall. Clinical examinations of the skin were conducted by dermatologists. Skin-aging appearance was defined as having a wrinkled appearance, senile dryness, and skin atrophy.

RESULTS:
Higher vitamin C intakes were associated with a lower likelihood of a wrinkled appearance [odds ratio (OR) 0.89; 95% CI: 0.82, 0.96] and senile dryness (OR: 0.93;95%CI: 0.87, 0.99). Higher linoleic acid intakes were associated with a lower likelihood of senile dryness (OR: 0.75; 95% CI: 0.64, 0.88) and skin atrophy (OR: 0.78; 95% CI 0.65, 0.95). A 17-g increase in fat and a 50-g increase in carbohydrate intakes increased the likelihood of a wrinkled appearance (OR: 1.28 and 1.36, respectively) and skin atrophy (OR: 1.37 and 1.33, respectively). These associations were independent of age, race, education, sunlight exposure, income, menopausal status, body mass index, supplement use, physical activity, and energy intake.

CONCLUSIONS:
Higher intakes of vitamin C and linoleic acid and lower intakes of fats and carbohydrates are associated with better skin-aging appearance. Promoting healthy dietary behaviors may have additional benefit for skin appearance in addition to other health outcomes in the population.

Source
Cosgrove MC et al. Dietary nutrient intakes and skin-aging appearance among middle-aged American women. Am J Clin Nutr 86:1225-31, 2007.

Vitamin D2 is as effective as vitamin D3 in maintaining circulating concentrations of 25-hydroxyvitamin D

ABSTRACT

CONTEXT:

Two reports suggested that vitamin D2 is less effective than vitamin D3 in maintaining vitamin D status.

OBJECTIVE:

Our objective was to determine whether vitamin D2 was less effective than vitamin D3 in maintaining serum 25-hydroxyvitamin D levels or increased the catabolism of 25-hydroxyvitamin D3.

SUBJECTS AND **DESIGN:**

This was a randomized, placebo-controlled, double-blinded study of healthy adults ages 18-84 yr who received placebo, 1000 IU vitamin D3, 1000 IU vitamin D2, or 500 IU vitamin D2 plus 500 IU vitamin D3 daily for 11 wk at the end of the winter.

RESULTS:

Sixty percent of the healthy adults were vitamin D deficient at the start of the study. The circulating levels of 25-hydroxyvitamin D (mean+/-sd) increased to the same extent in the groups that received 1000 IU daily as vitamin D2 (baseline 16.9+/-10.5 ng/ml; 11 wk 26.8+/-9.6 ng/ml), vitamin D3 (baseline 19.6+/-11.1 ng/ml; 11 wk 28.9+/-11.0 ng/ml), or a combination of 500 IU vitamin D2 and 500 IU vitamin D3 (baseline 20.2+/-10.4 ng/ml; 11 wk 28.4+/-7.7 ng/ml). The 25-hydroxyvitamin D3 levels did not change in the group that received 1000 IU vitamin D2 daily. The 1000 IU dose of vitamin D2 or vitamin D3 did not raise 25-hydroxyvitamin D levels in vitamin D-deficient subjects above 30 ng/ml.

CONCLUSION:

A 1000 IU dose of vitamin D2 daily was as effective as 1000 IU vitamin D3 in maintaining serum 25-hydroxyvitamin D levels and did not negatively influence serum 25-hydroxyvitamin D3 levels. Therefore, vitamin D2 is equally as effective as vitamin D3 in maintaining 25-hydroxyvitamin D status.

Source
Holick MF, et al. Vitamin D2 is as effective as vitamin D3 in maintaining circulating concentrations of 25-hydroxyvitamin D. J Clin Endocrinol Metab. 2008 Mar;93(3):677-81.

Skin aging and photoaging alter fatty acids composition, including 11,14,17-eicosatrienoic acid, in the epidermis of human skin

ABSTRACT

We investigated the alterations of major fatty acid components in epidermis by natural aging and photoaging processes, and by acute ultraviolet (UV) irradiation in human skin. Interestingly, we found that 11,14,17-eicosatrienoic acid (ETA), which is one of the omega-3 polyunsaturated acids, was significantly increased in photoaged human epidermis in vivo and also in the acutely UV-irradiated human skin in vivo, while it was significantly decreased in intrinsically aged human epidermis. The increased ETA content in the epidermis of photoaged human skin and acute UV-irradiated human skin is associated with enhanced expression of human elongase 1 and calcium-independent phophodiesterase A2. We demonstrated that ETA inhibited matrix metalloproteinase (MMP)-1 expression after UV-irradiation, and that inhibition of ETA synthesis using EPTC and NA-TCA, which are elongase inhibitors, increased MMP-1 expression. Therefore, our results suggest that the UV increases the ETA levels, which may have a photoprotective effect in the human skin.

Source
Kim EJ, et al. Skin aging and photoaging alter fatty acids composition, including 11,14,17-eicosatrienoic acid, in the epidermis of human skin. J Korean Med Sci. 2010 Jun;25(6):980-3. Epub 2010 May 24.

Omega-3 fatty acids effect on wound healing

ABSTRACT

Physiological events in the initial inflammatory stage of cutaneous wound healing influence subsequent stages. Proinflammatory cytokines coordinate molecular and cellular processes during the inflammatory stage. Polyunsaturated fatty acids (PUFA) alter proinflammatory cytokine production, but how this phenomenon specifically influences wound healing is not clearly understood. In the present study, effects of marine-derived omega-3 eicosapentaenoic and docosahexaenoic PUFA on proinflammatory cytokines in wound serum and time to complete healing in healthy, human skin were evaluated. We compared plasma fatty acid levels in two groups (N=30) at baseline and after 4 weeks of eicosapentaenoic/docosahexaenoic PUFA supplements (active) or placebo (control). Eight small blisters on participants' forearms were created. Proinflammatory cytokines interleukin-1beta (IL-1beta), IL-6, and tumor necrosis factor-alpha were quantified in blister fluid at 5 and 24 hours after creation. Wound area was calculated daily. Eicosapentaenoic and docosahexaenoic plasma fatty acid levels were significantly higher in the active group. Additionally, we found significantly higher IL-1beta levels in blister fluid in the active group and time to complete wound closure was somewhat longer. These results suggest that eicosapentaenoic and docosahexaenoic PUFA may increase proinflammatory cytokine production at wound sites and thus, depending on the clinical context, have noninvasive, therapeutic potential to affect cutaneous wound healing.

Source
McDaniel JC, et al. Omega-3 fatty acids effect on wound healing. Wound Repair Regen. 2008 May-Jun;16(3):337-45.

UVB photoprotection with antioxidants: effects of oral therapy with d-alphatocopherol and ascorbic acid on the minimal erythema dose

ABSTRACT
Ultraviolet radiation absorption is responsible for the production of free radicals in damaged cells. This side effect may be neutralized using antioxidant substances. It has been reported that ascorbic acid and d-alpha-tocopherol scavenge reactive oxygen species. In a single-blind controlled clinical trial we studied 45 healthy volunteers divided into three groups. Group 1 received d-alpha-tocopherol 1,200 I.U. daily; Group 2 ascorbic acid 2 g daily and Group 3 ascorbic acid 2 g plus d-alpha-tocopherol 1,200 I.U. daily. Treatment was sustained for one week. Before and after treatment, the minimal erythema dose was determined in all participants. The results show that the median minimal erythema dose increased from 60 to 65 mJ/cm2 in Group 1 and from 50 to 70 mJ/cm2 in Group 3. No modifications were observed in Group 2. We conclude that d-alpha-tocopherol prescribed in combination with ascorbic acid produces the best photoprotective effect.

Source
Mireles-Rocha H, et al. UVB photoprotection with antioxidants: effects of oral therapy with d-alphatocopherol and ascorbic acid on the minimal erythema dose. Acta Derm Venereol 82:21-4, 2002.

Randomized controlled trial of oral omega-3 PUFA in solar-simulated radiation-induced suppression of human cutaneous immune responses

ABSTRACT
BACKGROUND:
Skin cancer is a major public health concern, and the majority of cases are caused by solar ultraviolet radiation (UVR) exposure, which suppresses skin immunity. Omega-3 (n23) PUFAs protect against photoimmunosuppression and skin cancer in mice, but the impact in humans is unknown.

OBJECTIVES:
We hypothesized that EPA-rich n23 PUFA would abrogate photoimmunosuppression in humans. Therefore, a nutritional study was performed to assess the effect on UVR suppression of cutaneous cell-mediated immunity (CMI) reflected by nickel contact hypersensitivity (CHS).

DESIGN:
In a double-blind, randomized controlled study, 79 volunteers (nickel-allergic women, 22–60 y old, with phototype I or II) took 5 g n23 PUFA–containing lipid (70% EPA plus 10% DHA) or a control lipid daily for 3 mo. After supplementation, nickel was applied to 3 skin sites preexposed on 3 consecutive days to 1.9, 3.8, or 7.6 J/cm2 of solar-simulated radiation (SSR) and to 3 unexposed control sites. Nickel CHS responses were quantified after 72 h and the percentage of immunosuppression by SSR was calculated. Erythrocyte [red blood cell (RBC)] EPA was measured by using gas chromatography.

RESULTS:
SSR dose-related suppression of the nickel CHS response was observed in both groups. Photoimmunosuppression appeared less in the n23 PUFA group than in the control group (not statistically significant [mean difference (95% CI): 6.9% (22.1%, 15.9%)]). The difference was greatest at 3.8 J/cm2 SSR [mean difference: 11% (95% CI: 0.5%, 21.4%)]. Postsupplementation RBC EPA was 4-fold higher in the n23 PUFA group than in the control group (mean difference: 2.69% (95% CI: 2.23%, 3.14%), which confirmed the EPA bioavailability.

CONCLUSION:
Oral n23 PUFAs appear to abrogate photoimmunosuppression in human skin, providing additional support for their chemopreventive role; verification of study findings is required.

Source
Pilkington SM et al. Randomized controlled trial of oral omega-3 PUFA in solar-simulated radiation-induced suppression of human cutaneous immune responses. Am J Clin Nutr 97:646-52, 2013.

Unraveling hidden secrets: The role of vitamin D in skin aging

ABSTRACT
The skin is the only tissue in the human body that represents both a target tissue for biologically active vitamin D compounds including 1,25-dihydroxyvitamin D [1,25(OH)2D] and has the capacity for the synthesis of 1,25(OH)2D from 7-dehydrocholesterol (7-DHC). Recent findings indicate that the vitamin D endocrine system (VDES), besides multiple other important functions, regulates aging in many tissues, including skin. This concept is strongly supported by several independent studies in genetically modified mice (including FGF23(-/-) and Klotho(-/-) mice) that are characterized by altered mineral homeostasis caused by a high vitamin D activity. These mice typically have phenotypic features of premature aging that include, besides short lifespan, retarded growth, ectopic calcification, immunological deficiency, osteoporosis, atherosclerosis, hypogonadism, skin and general organ atrophy. Notably, it has been demonstrated that these phenotypic features can be reversed by normalizing mineral homeostasis and/or vitamin D status. Interestingly, the aging phenotypes of mice suffering from hypovitaminosis D (VDR(-/-) and CYP27B1(-/-) mice) are quite similar to those suffering from hypervitaminosis D (including FGF-23(-/-) and Klotho(-/-) mice).

Consequently, it has been hypothesized that thus, both hypo- and hypervitaminosis D may enhance aging. Aging seems to show a U-shaped response curve to vitamin D status, and, therefore normovitaminosis D seems to be important for preventing premature aging. Additionally, laboratory investigations have now convincingly shown that vitamin D compounds protect the skin against the hazardous effects of various skin aging-inducing agents, including ultraviolet (UV) radiation. In conclusion, these findings support the concept that UV-radiation exerts both skin aging -promoting and -inhibiting effects, the latter via induction of cutaneous vitamin D synthesis. Future studies will clarify the effect of vitamin D compounds on expression and function of potential key regulators of skin aging, such as TAp63 or the IGF-1 signaling pathway. Furthermore, the efficacy of topically applied vitamin D compounds in the prevention of skin aging has to be evaluated in future clinical trials.

Source
Reichrath J. Unraveling hidden secrets: The role of vitamin D in skin aging. Dermato-Endocrinolgoy 43:241-44, 2012.

Botanicals in Dermatology: An Evidence based Review

ABSTRACT
Botanical extracts and single compounds are increasingly used in cosmetics but also in over-the-counter drugs and food supplements. The focus of the present review is on controlled clinical trials with botanicals in the treatment of acne, inflammatory skin diseases, skin infections, UV-induced skin damage, skin cancer, alopecia, vitiligo, and wounds. Studies with botanical cosmetics and drugs are discussed, as well as studies with botanical food supplements. Experimental research on botanicals was considered to a limited extent when it seemed promising for clinical use in the near future. In acne therapy, Mahonia, tea tree oil, and Saccharomyces may have the potential to become standard treatments. Mahonia, Hypericum, Glycyrrhiza and some traditional Chinese medicines appear promising for atopic dermatitis. Some plant-derived substances like dithranol and methoxsalen (8-methoxypsoralen) [in combination with UVA] are already accepted as standard treatments in psoriasis; Mahonia and Capsicum (capsaicin) are the next candidates suggested by present evidence. Oral administration and topical application of antioxidant plant extracts (green and black tea, carotenoids, coffee, and many flavonoids from fruits and vegetables) can protect skin from UV-induced erythema, early aging, and irradiation-induced cancer. Hair loss and vitiligo are also traditional fields of application for botanicals. According to the number and quality of clinical trials with botanicals, the best evidence exists for the treatment of inflammatory skin diseases, i.e. atopic dermatitis and psoriasis. However, many more controlled clinical studies are needed to determine the efficacy and risks of plant-derived products in dermatology. Safety aspects, especially related to sensitization and photodermatitis, have to be taken into account. Therefore, clinicians should not only be informed of the beneficial effects but also the specific adverse effects of botanicals used for dermatologic disorders and cosmetic purposes.

Source
Reuter J et al. Botanicals in Dermatology: An Evidence based Review. Am J Clin Dermatol 11:247-67, 2010.

Oral green tea catechin metabolites are incorporated into human skin and protect against UV radiation-induced cutaneous inflammation in association with reduced production of pro-inflammatory eicosanoid 12-hydroxyeicosatetraenoic acid

ABSTRACT
Green tea catechins (GTC) reduce UV radiation (UVR)-induced inflammation in experimental models, but human studies are scarce and their cutaneous bioavailability and mechanism of photoprotection are unknown. We aimed to examine oral GTC cutaneous uptake, ability to protect human skin against erythema induced by a UVR dose range and impact on potent cyclo-oxygenase- and lipoxygenase-produced mediators of UVR inflammation, PGE2 and 12-hydroxyeicosatetraenoic acid (12-HETE), respectively. In an open oral intervention study, sixteen healthy human subjects (phototype I/II) were given low-dose GTC (540 mg) with vitamin C (50 mg) daily for 12 weeks. Pre- and post-supplementation, the buttock skin was exposed to UVR and the resultant erythema quantified. Skin blister fluid and biopsies were taken from the unexposed and the UVR-exposed skin 24 h after a pro-inflammatory UVR challenge (three minimal erythema doses). Urine, skin tissue and fluid were analysed for catechin content and skin fluid for PGE2 and 12-HETE by liquid chromatography coupled to tandem MS. A total of fourteen completing subjects were supplement compliant (twelve female, median 42.5 years, range 29-59 years). Benzoic acid levels were increased in skin fluid post-supplementation (P= 0.03), and methylated gallic acid and several intact catechins and hydroxyphenyl-valerolactones were detected in the skin tissue and fluid. AUC analysis for UVR erythema revealed reduced response post-GTC (P= 0.037). Pre-supplementation, PGE2 and 12-HETE were UVR induced (P= 0.003, 0.0001). After GTC, UVR-induced 12-HETE reduced from mean 64 (sd 42) to 41 (sd 32) pg/μl (P= 0.01), while PGE2 was unaltered. Thus, GTC intake results in the incorporation of catechin metabolites into human skin associated with abrogated UVR-induced 12-HETE; this may contribute to protection against sunburn inflammation and potentially longer-term UVR-mediated damage.

Source
Rhodes LE et al. Oral green tea catechin metabolites are incorporated into human

skin and protect against UV radiation-induced cutaneous inflammation in association with reduced production of pro-inflammatory eicosanoid 12-hydroxyeicosatetraenoic acid. Br

Significant correlations of dermal total carotenoids and dermal lycopene with their respective plasma levels in healthy adults

ABSTRACT
Carotenoids in skin have been known to play a role in photoprotection against UV radiation. We performed dermal biopsies of healthy humans (N=27) and collected blood samples for pair-wise correlation analyses of total and individual carotenoid content by high performance liquid chromatography (HPLC). The hydrocarbon carotenoids (lycopene and beta-carotene) made up the majority of carotenoids in both skin and plasma, and skin was somewhat enriched in these carotenoids relative to plasma. Beta-cryptoxanthin, a monohydroxycarotenoid, was found in similar proportions in skin as in plasma. In contrast, the dihydroxycarotenoids, lutein and zeaxanthin, were relatively lacking in human skin in absolute and relative levels as compared to plasma. Total carotenoids were significantly correlated in skin and plasma ($r = 0.53$, $p<0.01$). Our findings suggest that human skin is relatively enriched in lycopene and beta-carotene, compared to lutein and zeaxanthin, possibly reflecting a specific function of hydrocarbon carotenoids in human skin photoprotection.

Source
Scarmo S et al. Significant correlations of dermal total carotenoids and dermal lycopene with their respective plasma levels in healthy adults. Arch Biochem Biophys 504:34-39, 2010.

Discovering the link between nutrition and skin aging

ABSTRACT
Skin has been reported to reflect the general inner-health status and aging. Nutrition and its reflection on skin has always been an interesting topic for scientists and physicians throughout the centuries worldwide. Vitamins, carotenoids, tocopherols, flavonoids and a variety of plant extracts have been reported to possess potent anti-oxidant properties and have been widely used in the skin care industry either as topically applied agents or oral supplements in an attempt to prolong youthful skin appearance. This review will provide an overview of the current literature “linking” nutrition with skin aging.

Source
Schagen S et al. Discovering the link between nutrition and skin aging. Review. Dermato-Endocrinol 4:298-307, 2012.

Photoprotection by dietary carotenoids: concept, mechanisms, evidence and future development

ABSTRACT
Carotenoids are micronutrients present mainly in fruits and vegetables, and they are ingested from these sources with the diet. They exhibit specific antioxidant activity but also influence signaling and gene expression at the cellular level. β-Carotene and lycopene, the colorants of carrots and tomatoes, respectively, are among the most prominent members of this group of lipids, and they are usually the dominating carotenoids in human blood and tissues. Both compounds modulate skin properties when ingested as supplements or as dietary products. There is evidence that they protect the skin against sunburn (solar erythema) by increasing the basal defense against UV light-mediated damage. Their photoprotective efficacy, however, is not comparable to the use of a sunscreen. In vitro data show that also other carotenoids are efficient photoprotectors. Among them are lutein and structurally unusual phenolic polyenes like 3,3 -dihydroxyisorenieratene.

Source
Stahl W and Sies H. Photoprotection by dietary carotenoids: concept, mechanisms, evidence and future development. Mol Nutr Food Res 56:287-95, 2012.

Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans

ABSTRACT
BACKGROUND:
Carotenoids and tocopherols, known to be efficient antioxidants and capable of scavenging reactive oxygen species generated during photooxidative stress, may protect the skin from ultraviolet light–induced erythema. b-Carotene is widely used as an oral sun protectant but studies on its protective effects are scarce.

OBJECTIVE:
The objective of this study was to investigate the protective effects of oral supplementation with carotenoids and a combination of carotenoids and vitamin E against the development of erythema in humans.

DESIGN:
A carotenoid supplement (25 mg total carotenoids/d) and a combination of the carotenoid supplement and vitamin E [335 mg (500 IU) RRR-a-tocopherol/d] were given for 12 wk to healthy volunteers. Erythema was induced by illumination with a blue-light solar simulator. Serum b-carotene and a-tocopherol concentrations and skin carotenoid levels were assessed by HPLC and reflection photometry.

RESULTS:
Serum b-carotene and a-tocopherol concentrations increased with supplementation. Erythema on dorsal skin (back) was significantly diminished ($P < 0.01$) after week 8, and erythema suppression was greater with the combination of carotenoids and vitamin

E than with carotenoids alone.

CONCLUSION:
The antioxidants used in this study provided protection against erythema in humans and may be useful for diminishing sensitivity to ultraviolet light.

Source
Stahl, W et al. Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans. Am J Clin Nutr 71:795-8, 2000.

A randomized controlled trial of an appearance-based dietary intervention

ABSTRACT
OBJECTIVE:
Inadequate fruit and vegetable consumption precipitates preventable morbidity and mortality. The efficacy of an appearance-based-dietary intervention was investigated, which illustrates the beneficial effect that fruit and vegetable consumption has on skin appearance.

METHODS:

Participants were randomly allocated to three groups receiving information-only or a generic or own-face appearance-based intervention. Diet was recorded at baseline and 10 weekly follow-ups. Participants in the generic and own-face intervention groups witnessed on-screen stimuli and received printed photographic materials to illustrate the beneficial effect of fruit and vegetable consumption on skin color.

RESULTS:
Controlling for baseline diet, a significant effect of intervention group was found on self-reported fruit and vegetable intake among 46 completers who were free of medical and personal reasons preventing diet change. The own-face appearance-based intervention group reported a significant, sustained improvement in fruit and vegetable consumption whereas the information-only and generic appearance-based intervention groups reported no significant dietary changes.

CONCLUSIONS:
Seeing the potential benefits of fruit and vegetable consumption on own skin color may motivate dietary improvement.

Source
Whitehead RD et al. A randomized controlled trial of an appearance-based dietary intervention. Health Psychol, Epub ahead of print, 2013.

You are what you eat: Within-subject increases in fruit and vegetable consumption confer beneficial skin-color changes

ABSTRACT
BACKGROUND:
Fruit and vegetable consumption and ingestion of carotenoids have been found to be associated with human skin-color (yellowness) in a recent cross-sectional study. This carotenoid-based coloration contributes beneficially to the appearance of health in humans and is held to be a sexually selected cue of condition in other species.

METHODOLOGY AND PRINCIPAL FINDINGS:
Here we investigate the effects of fruit and vegetable consumption on skin-color longitudinally to determine the magnitude and duration of diet change required to change skin-color perceptibly. Diet and skin-color were recorded at baseline and after three and six weeks, in a group of 35 individuals who were without makeup, self-tanning agents and/or recent intensive UV exposure. Six-week changes in fruit and vegetable consumption were significantly correlated with changes in skin redness and yellowness over this period, and diet-linked skin reflectance changes were significantly associated with the spectral absorption of carotenoids and not melanin. We also used psychophysical methods to investigate the minimum color change required to confer perceptibly healthier and more attractive skin-coloration. Modest dietary changes are required to enhance apparent health (2.91 portions per day) and attractiveness (3.30 portions).

CONCLUSIONS:
Increased fruit and vegetable consumption confers measurable and perceptibly beneficial effects on Caucasian skin appearance within six weeks. This effect could potentially be used as a motivational tool in dietary intervention.

Source
Whitehead RD et al. You are what you eat: Within-subject increases in fruit and vegetable consumption confer beneficial skin-color changes. PLoS ONE 7:e32988, 2012.

SPORTS NUTRITION

The Role of Nutritional Supplements in the Prevention and Treatment of Resistance-Induced Skeletal Muscle Injury

ABSTRACT
The topic of exercise-induced skeletal muscle injury has received considerable attention in recent years. Likewise, strategies to minimise the injury resulting from heavy resistance exercise have been studied. Over the past 15 years, several investigations have been performed focused on the role of nutritional supplements to attenuate signs and symptoms of muscle injury. Of these, some have reported favourable results, while many others have reported no benefit of the selected nutrient. Despite these mixed findings, recommendations for the use of nutritional supplements for the purposes of attenuating muscle injury are rampant within the popular fitness media and athletic world, largely without scientific support. Those nutrients include the antioxidant vitamin C (ascorbic acid) and vitamin E (tocopherol), N-acetyl-cysteine, flavonoids, L-carnitine, astaxanthin, beta-hydroxy-beta-methylbutyrate, creatine monohydrate, essential fatty acids, branched-chain amino acids, bromelain, proteins and carbohydrates. A discussion of all published peer-

reviewed articles in reference to these nutrients and their impact on resistance exercise-induced skeletal muscle injury is presented, in addition to a brief view into the potential mechanism of action for each nutrient.Based on the current state of knowledge, the following conclusions can be made with regard to nutritional supplements and their role in attenuating signs and symptoms of skeletal muscle injury occurring as a consequence of heavy resistance exercise: (i) there appears to be a potential role for certain supplements (vitamin C, vitamin E, flavonoids, and L-carnitine); (ii) these supplements cannot effectively eliminate muscle injury, only attenuate certain signs and symptoms; (iii) it is presently unclear what the optimal dosage of these nutrients is (whether used alone or in combination); (iv) it is unclear what the optimal pretreatment period is; and (v) the effectiveness is largely specific to non-resistance trained individuals.Ultimately, because so few studies have been conducted in this area, it is difficult to recommend with confidence the use of selected nutrients for the sole purpose of minimising signs and symptoms of resistance exercise-induced muscle injury, in particular with regard to resistance-trained individuals.

Source
Bloomer R, et al; The Role of Nutritional Supplements in the Prevention and Treatment of Resistance-Induced Skeletal Muscle Injury. Sports Medicine, 2007.

The effects of omega-3 supplementation on pulmonary function of young wrestlers during intensive training

ABSTRACT
The purpose of this study was to examine the effects of omega-3 supplementation on young wrestler's pulmonary function during intensive wrestling training. Forty healthy young male wrestlers participated in this study. The subjects were randomly divided into experimental (n=10), placebo (n=10), active control (n=10) and inactive control (n=10) groups. Participants in experimental, placebo and active control groups performed wrestling incremental training up to 95% of exercise MHR, three times a week, for 12 weeks. The inactive control group did not participate in any exercisetraining. Subjects in the experimental group were asked to consume omega-3 (1000 mg/day for 12 weeks), while those in placebo were refused any doses of omega-3. The pulmonary variables were measured at baseline and at the end of 12 weeks of training program. Results indicated that consuming omega-3 during 12 weeks training had a significantly positive effect on pulmonary variables such as FEV1, FVC, VC, MVV, FEF25-75, FIV1 (p=0.001), but no significant changes were observed in FEV1% (p=0.141) and FIV1% (p=0.117). The results of the present study suggest that consuming omega-3 during intensive wrestling training can improve pulmonary function of athletes during and in post-exercise.

Source
Tartibian B, et al. The effects of omega-3 supplementation on pulmonary function of young wrestlers during intensive training. J Sci Med Sport. 2010 Mar;13(2):281-6.

STRESS MANAGEMENT

Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial

ABSTRACT
Observational studies have linked lower omega-3 (n-3) polyunsaturated fatty acids (PUFAs) and higher omega-6 (n-6) PUFAs with inflammation and depression, but randomized controlled trial (RCT) data have been mixed. To determine whether n-3 decreases proinflammatory cytokine production and depressive and anxiety symptoms in healthy young adults, this parallel group, placebo-controlled, double-blind 12-week RCT compared n-3 supplementation with placebo. The participants, 68 medical students, provided serial blood samples during lower-stress periods as well as on days before an exam. The students received either n-3 (2.5 g/d, 2085 mg eicosapentaenoic acid and 348 mg docosahexanoic acid) or placebo capsules that mirrored the proportions of fatty acids in the typical American diet. Compared to controls, those students who received n-3 showed a 14% decrease in lipopolysaccharide (LPS) stimulated interleukin 6 (IL-6) production and a 20% reduction in anxiety symptoms, without significant change in depressive symptoms. Individuals differ in absorption and metabolism of n-3 PUFA supplements, as well as in adherence; accordingly, planned secondary analyses that used the plasma n-6:n-3 ratio in place of treatment group showed that decreasing n-6:n-3 ratios led to lower anxiety and reductions in stimulated IL-6 and tumor necrosis factor alpha (TNF-α) production, as well as marginal differences in serum TNF-α. These data suggest that n-3 supplementation can reduce inflammation and anxiety even among healthy young adults. The reduction in anxiety symptoms associated with n-3 supplementation provides the first evidence that n-3 may have potential anxiolytic benefits for individuals without an anxiety disorder diagnosis.

Source
Kiecolt-Glaser JK et al. Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial. Brain Behav Immun 25:1725-34, 2011.

WEIGHT MANAGEMENT

Vitamin D status and its relation to muscle mass and muscle fat in young women

ABSTRACT

CONTEXT:
Vitamin D insufficiency has now reached epidemic proportions and has been linked to increased body fat and decreased muscle strength. Whether vitamin D insufficiency is also related to adipose tissue infiltration in muscle is not known.

OBJECTIVE:
The objective of the study was to examine the relationship between serum 25-hydroxyvitamin D (25OHD) and the degree of fat infiltration in muscle.

DESIGN:
This was a cross-sectional study.

OUTCOME MEASURES AND SUBJECTS:
Measures were anthropometric measures, serum 25OHD radioimmunoassay values, and computed tomography (CT) values of fat, muscle mass, and percent muscle fat in 90 postpubertal females, aged 16-22 yr, residing in California.

RESULTS:
Approximately 59% of subjects were 25OHD insufficient (< or = 29 ng/ml), of which 24% were deficient (< or = 20 ng/ml), whereas 41% were sufficient (> or = 30 ng/ml). A strong negative relationship was present between serum 25OHD and CT measures of percent muscle fat (r = -0.37; P < 0.001). In contrast, no relationship was observed between circulating 25OHD concentrations and CT measures of thigh muscle area (r = 0.16; P = 0.14). Multiple regression analysis indicated that the relation between 25OHD and muscle adiposity was independent of body mass or CT measures of sc and visceral fat. Percent muscle fat was significantly lower in women with normal serum 25OHD concentrations than in women with insufficient levels and deficient levels (3.15 +/- 1.4 vs. 3.90 +/- 1.9; P = 0.038).

CONCLUSIONS:
We found that vitamin D insufficiency is associated with increased fat infiltration in muscle in healthy young women.

Source
Gilsanz V, et al. Vitamin D status and its relation to muscle mass and muscle fat in young women. J Clin Endocrinol Metab. 2010 Apr;95(4):1595-601.

Serum 25-Hydroxyvitamin D is Independently Associated with High Density Lipoprotein Cholesterol and the Metabolic Syndrome in Men and Women

ABSTRACT

BACKGROUND:
Low vitamin D status has been associated with markers of cardiovascular disease risk.

OBJECTIVE:
This cross-sectional study assessed the relationships between serum 25-hydroxyvitamin D [25(OH)D] and selected markers for cardiovascular disease risk, including metabolic syndrome and its components, in adult men and women.

METHODS:
Fasting blood samples, anthropometric measurements, and blood pressure were assessed in 257 men and women. Dietary intake was assessed with food frequency and dietary supplement questionnaires.

RESULTS:
Total vitamin D intake and that from dietary supplements were significantly associated with increasing serum 25(OH)D tertile (both P < .001). Mean±SEM serum high-density lipoprotein cholesterol (HDL-C) increased in a graded fashion (P < .001) from the lowest (48.4±1.8mg/dL) to the highest (62.3±2.1mg/dL) 25(OH)D tertile. The relationship between 25(OH)D and HDL-C remained significant (P < .001) after adjustment for established determinants of the HDL-C, with each 10-ng/mL increase in 25(OH)D associated with a 4.2-mg/dL increase in HDL-C concentration. Serum triglycerides (P=.008), waist circumference (P < .001), and body mass index (P < .001) showed graded, inverse relationships with 25(OH)D tertile, and the prevalence of metabolic syndrome decreased significantly from the lowest to the highest 25(OH)D tertile (31%, 14%, and 10%, respectively, P for trend=.001).

CONCLUSIONS:
Lower serum 25(OH)D is associated with the metabolic syndrome and adverse values for some metabolic syndrome risk factors, particularly the HDL-C concentration. Research is warranted to assess whether increasing vitamin D intake will improve the metabolic cardiovascular risk factor profile.

Source
Maki KC, et al. Serum 25-Hydroxyvitamin D is Independently Associated with High Density Lipoprotein Cholesterol and the Metabolic Syndrome in Men and Women. J Clin Lipidology. 2009 Jul; 3(4):289-96

Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study

ABSTRACT

BACKGROUND:
Observational studies have linked higher intakes of whole grains to lower abdominal adiposity; however, the association between whole- and refined-grain intake and body fat compartments has yet to be reported.

OBJECTIVE:
Different aspects of diet may be differentially related to body fat distribution. The purpose of this study was to assess associations between whole- and refined-grain intake and abdominal subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT).

DESIGN:
Cross-sectional associations between whole- and refined-grain intakes, waist circumference measures, and abdominal SAT and VAT volumes were examined in 2834 Framingham Heart Study participants

(49.4% women; age range: 32-83 y). Dietary information was assessed with the use of a semiquantitative food-frequency questionnaire.

RESULTS:
Whole-grain intake was inversely associated with SAT (2895 compared with 2552 cm^3 in the lowest compared with the highest quintile category, P for trend < 0.001) and VAT (1883 compared with 1563 cm^3, P for trend < 0.001), after adjustment for age, sex, current smoking status, total energy, and alcohol intake. In contrast, refined-grain intake was positively associated with SAT (2748 compared with 2934 cm^3, P for trend = 0.01) and VAT (1727 compared with 1928 cm^3, P for trend < 0.001) in multivariable models. When SAT and VAT were evaluated jointly, the P value for SAT was attenuated (P = 0.28 for whole grains, P = 0.60 for refined grains), whereas VAT remained associated with both whole grains (P < 0.001) and refined grains (P < 0.001).

CONCLUSIONS:
Increasing whole-grain intake is associated with lower VAT in adults, whereas higher intakes of refined grains are associated with higher VAT. Further research is required to elicit the potential mechanisms whereby whole- and refined-grain foods may influence body fat distribution.

Source
McKeown NM, et al. Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study. Am J Clin Nutr. 2010 Nov;92(5):1165-71. Epub 2010 Sep 29.

Calcium and vitamin D supplementation is associated with decreased abdominal visceral adipose tissue in overweight and obese adults

ABSTRACT
BACKGROUND:
Several studies suggest that calcium and vitamin D (CaD) may play a role in the regulation of abdominal fat mass.

OBJECTIVE:
This study investigated the effect of CaD-supplemented orange juice (OJ) on weight loss and reduction of visceral adipose tissue (VAT) in overweight and obese adults (mean ± SD age: 40.0 ± 12.9 y).

DESIGN:
Two parallel, double-blind, placebo-controlled trials were conducted with either regular or reduced-energy (lite) orange juice. For each 16-wk trial, 171 participants were randomly assigned to 1 of 2 groups. The treatment groups consumed three 240-mL glasses of OJ (regular or lite) fortified with 350 mg Ca and 100 IU vitamin D per serving, and the control groups consumed either unfortified regular or lite OJ. Computed tomography scans of VAT and subcutaneous adipose tissue were performed by imaging a single cut at the lumbar 4 level.

RESULTS:
After 16 wk, the average weight loss (2.45 kg) did not differ significantly between groups. In the regular OJ trial, the reduction of VAT was significantly greater (P = 0.024) in the CaD group (-12.7 ± 25.0 cm(2)) than in the control group (-1.3 ± 13.6 cm(2)). In the lite OJ trial, the reduction of VAT was significantly greater (P = 0.039) in the CaD group (-13.1 ± 18.4 cm(2)) than in the control group (-6.4 ± 17.5 cm(2)) after control for baseline VAT. The effect of calcium and vitamin D on VAT remained highly significant when the results of the 2 trials were combined (P = 0.007).

CONCLUSIONS:
The findings suggest that calcium and/or vitamin D supplementation contributes to a beneficial reduction of VAT. This trial is registered at clinicaltrial.gov as NCT00386672, NCT01363115.

Source
Rosenblum JL et al. Calcium and vitamin D supplementation is associated with decreased abdominal visceral adipose tissue in overweight and obese adults. Am J Clin Nutr 95:101-8, 2011.

Dietary omega 3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial

ABSTRACT
BACKGROUND:
Loss of muscle mass with aging is a major public health concern. Omega-3 (n–3) fatty acids stimulate protein anabolism in animals and might therefore be useful for the treatment of sarcopenia. However, the effect of omega-3 fatty acids on human protein metabolism is unknown.

OBJECTIVE:
The objective of this study was to evaluate the effect of omega-3 fatty acid supplementation on the rate of muscle protein synthesis in older adults.

DESIGN:
Sixteen healthy, older adults were randomly assigned to receive either omega-3 fatty acids or corn oil for 8 wk. The rate of muscle protein synthesis and the phosphorylation of key elements of the anabolic signaling pathway were evaluated before and after supplementation during basal, postabsorptive conditions and during a hyperaminoacidemic-hyperinsulinemic clamp.

RESULTS:
Corn oil supplementation had no effect on the muscle protein synthesis rate and the extent of anabolic signaling element phosphorylation in muscle. Omega-3 fatty acid supplementation had no effect on the basal rate of muscle protein synthesis (mean 6 SEM: 0.051 6 0.005%/h compared with 0.053 6 0.008%/h before and after supplementation, respectively; P = 0.80) but augmented the hyperaminoacidemia-hyperinsulinemia–induced increase in the rate of muscle protein synthesis (from 0.009 6 0.005%/h above basal values to 0.031 6 0.003%/h above basal values; P , 0.01), which was accompanied by greater increases in muscle mTORSer2448 (P = 0.08) and p70s6kThr389 (P , 0.01) phosphorylation.

CONCLUSION:
Omega-3 fatty acids stimulate muscle protein synthesis in older adults and may be useful for the prevention and treatment of sarcopenia.

Source
Smith GI, Atherton P, Reeds DN et al. Dietary omega 3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial. Am J Clin Nutr 2011;93:402-12.

Greater Whole-Grain Intake Is Associated with Lower Risk of Type 2 Diabetes, Cardiovascular Disease, and Weight Gain

ABSTRACT
Whole-grain and high fiber intakes are routinely recommended for prevention of vascular diseases; however, there are no comprehensive and quantitative assessments of available data in humans. The aim of this study was to systematically examine longitudinal studies investigating whole-grain and fiber intake in relation to risk of type 2 diabetes (T2D), cardiovascular disease (CVD), weight gain, and metabolic risk factors. We identified 45 prospective cohort studies and 21 randomized-controlled trials (RCT) between 1966 and February 2012 by searching the Cumulative Index to Nursing and Allied Health Literature, Cochrane, Elsevier Medical Database, and PubMed. Study characteristics, whole-grain and dietary fiber intakes, and risk estimates were extracted using a standardized protocol. Using random effects models, we found that compared with never/rare consumers of whole grains, those consuming 48-80 g whole grain/d (3-5 serving/d) had an ~26% lower risk of T2D [RR = 0.74 (95% CI: 0.69, 0.80)], ~21% lower risk of CVD [RR = 0.79 (95% CI: 0.74, 0.85)], and consistently less weight gain during 8-13 y (1.27 vs 1.64 kg; P = 0.001). Among RCT, weighted mean differences in post-intervention circulating concentrations of fasting glucose and total and LDL-cholesterol comparing whole-grain intervention groups with controls indicated significantly lower concentrations after whole-grain interventions [differences in fasting glucose: -0.93 mmol/L (95% CI: -1.65, -0.21), total cholesterol: -0.83 mmol/L (-1.23, -0.42); and LDL-cholesterol: -0.82 mmol/L (-1.31, -0.33)]. [corrected] Findings from this meta-analysis provide evidence to support beneficial effects of whole-grain intake on vascular disease prevention. Potential mechanisms responsible for whole grains' effects on metabolic intermediates require further investigation in large intervention trials.

Source
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