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TABLE OF CONTENTS

Peer Reviewed Studies.....2
Blood Sugar Balance 2
Bone and Joint Health.....4
Cellular Health.....7
Children's Health.....8
Cognitive Health.....9
Digestive Health.....9
Eye Health.....10
Healthy Pregnancy 10
Heart Health.....11
Immune Health 15
Prostate Health 17
Skin Health.....18
Weight Management.....18

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PEER REVIEWED STUDIES

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.

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.

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 supplements combined (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). This trial was registered at clinicaltrials.gov as NCT00436475.

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

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

ABSTRACT

BACKGROUND & AIMS:
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 68 517 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.

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.

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.

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.

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.

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.

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]

CELLULAR HEALTH

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.

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.

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). This trial was registered at clinicaltrials.gov as NCT00436475.

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

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.

Role of calcium during pregnancy: maternal and fetal needs

ABSTRACT

Although the demand for additional calcium during pregnancy is recognized, the dietary reference intake for calcium was lowered for pregnant women in 1997 to amounts recommended for nonpregnant women (1,000 mg/day), and recently (November 2010) the Institute of Medicine report upheld the 1997 recommendation. It has been frequently reported that women of childbearing age do not consume the dietary reference intake for calcium and that calcium intake in the United States varies among ethnic groups. Women who chronically consume suboptimal amounts of calcium (<500 mg/day) may be at risk for increased bone loss during pregnancy. Women who begin pregnancy with adequate intake may not need additional calcium, but women with suboptimal intakes (<500 mg) may need additional amounts to meet both maternal and fetal bone requirements. The objective of this review is to elucidate the changes in calcium metabolism that occur during pregnancy as well as the effect of maternal calcium intake on both maternal and fetal outcomes.

Source

Hacker AN, Fung EB, King JC. Role of calcium during pregnancy: maternal and fetal needs. Nutrition Reviews 2012 Jul;70(7):397-409.

COGNITIVE HEALTH

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 of cognitive impairment.

Source

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

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 lowermost 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

Vitamin D status and early age related macular degeneration in postmenopausal women

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

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.

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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.

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Role of calcium during pregnancy: maternal and fetal needs

ABSTRACT
Although the demand for additional calcium during pregnancy is recognized, the dietary reference intake for calcium was lowered for pregnant women in 1997 to amounts recommended for nonpregnant women (1,000 mg/day), and recently (November 2010) the Institute of Medicine report upheld the 1997 recommendation. It has been frequently reported that women of childbearing age do not consume the dietary reference intake for calcium and that calcium intake in the United States varies among ethnic groups. Women who chronically consume suboptimal amounts of calcium (<500 mg/day) may be at risk for increased bone loss during pregnancy. Women who begin pregnancy with adequate intake may not need additional calcium, but women with suboptimal intakes (<500 mg) may need additional amounts to meet both maternal and fetal bone requirements. The objective of this review is to elucidate the changes in calcium metabolism that occur during pregnancy as well as the effect of maternal calcium intake on both maternal and fetal outcomes.

Source
Hacker AN, Fung EB, King JC. Role of calcium during pregnancy: maternal and fetal needs. Nutrition Reviews 2012 Jul;70(7):397-409.

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.

HEART HEALTH

Calcium supplementation for the management of primary hypertension in adults

ABSTRACT
BACKGROUND:
Metabolic studies suggest calcium may have a role in the regulation of blood pressure. Some epidemiological studies have reported that people with a higher intake of calcium tend to have lower blood pressure. Previous systematic reviews and meta-analyses have reached conflicting conclusions about whether oral calcium supplementation can reduce blood pressure.

OBJECTIVES:
To evaluate the effects of oral calcium supplementation as a treatment for primary hypertension in adults.

SEARCH STRATEGY:
We searched the Cochrane Library, MEDLINE, EMBASE, Science Citation Index, ISI Proceedings, ClinicalTrials.gov, Current Controlled Trials, CAB abstracts, and reference lists of systematic reviews, meta-analyses and randomised controlled trials (RCTs) included in the review.

SELECTION CRITERIA:
Inclusion criteria were: 1) RCTs comparing oral calcium supplementation with placebo, no treatment, or usual care; 2) treatment and follow-up >/=8 weeks; 3) participants over 18 years old, with raised systolic blood pressure (SBP) >/=140 mmHg or diastolic blood pressure (DBP) >/=85 mmHg; 4) SBP and DBP reported at end of follow-up. We excluded trials where: participants were pregnant; received antihypertensive medication which changed during the study; or calcium supplementation was combined with other interventions.

DATA COLLECTION AND ANALYSIS:
Two reviewers independently abstracted data and assessed trial quality. Disagreements were resolved by discussion or a third reviewer. Random effects meta-analyses and sensitivity analyses were conducted.

MAIN RESULTS:
We included 13 RCTs (n=485), with between eight and 15 weeks follow-up. The results of the individual trials were heterogeneous. Combining all trials, participants receiving calcium supplementation as compared to control had a statistically significant reduction in SBP (mean difference: -2.5 mmHg, 95% CI: -4.5 to -0.6, I(2)= 42%), but not DBP (mean difference: -0.8 mmHg, 95% CI: -2.1 to 0.4, I(2) = 48%). Sub-group analyses indicated that heterogeneity between trials could not be explained by dose of calcium or baseline blood pressure. Heterogeneity was reduced when poor quality trials were excluded. The one trial reporting adequate concealment of allocation and the one trial reporting adequate blinding yielded results consistent with the primary meta-analysis.

AUTHORS' CONCLUSIONS:
In view of the poor quality of included trials and the heterogeneity between trials, the evidence in favour of causal association between calcium supplementation and blood pressure reduction is weak and is probably due to bias. This is because poor quality studies generally tend to over-estimate the effects of treatment. Larger, longer duration and better quality double-blind placebo controlled trials are needed to assess the effect of calcium supplementation on blood pressure and cardiovascular outcomes.

Source
Dickinson HO, et al. Calcium supplementation for the management of primary hypertension in adults. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD004639.

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

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

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.

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 adiposetissue (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.

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.

IMMUNE HEALTH

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.

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.

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.

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.

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.

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.

PROSTATE 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 noncompetitive 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

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

SKIN HEALTH

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.

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.

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.

Efficacy of calcium supplementation for management of overweight and obesity: A systematic review of randomized trials

ABSTRACT
Numerous dietary supplements are marketed as slimming aids, but the efficacy of most has not been proven. One such slimming aid is calcium. Presented here are the results of a systematic review that aimed to evaluate the evidence for or against the efficacy of calcium supplements for body-weight reduction in overweight and obese individuals. Electronic searches were conducted to identify relevant randomized clinical trials of at least 6 months duration. No restrictions of age, gender, language, or time of publication were imposed. Two reviewers independently determined the eligibility of studies, assessed the reporting quality of the studies included, and extracted data. Twenty-four eligible trials were identified, and seven were included. Five of the randomized clinical trials included were not of good reporting quality. A meta-analysis revealed a small, significant reduction in body weight for calcium compared with placebo (mean difference, (-) 0.74 kg; 95% confidence interval, (-) 1.00-(-) 0.48). A small, significant reduction in body fat favoring calcium over placebo was also noted (mean difference, (-) 0.93 kg; 95% confidence interval, (-) 1.16-(-) 0.71). In conclusion, the evidence from randomized clinical trials suggests calcium supplementation generates small, statistically significant weight loss in overweight and obese individuals, but the clinical relevance of this finding is uncertain.

Source
Onakpoya IJ et al. Efficacy of calcium supplementation for management of overweight and obesity: A systematic review of randomized trials. Nutr Rev 69:335-43, 2011.

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 adiposetissue (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.