## Diabetes Mellitus
## Plasma/Serum Lycopene and Disease Risk

| Disease type | First Author | Study Title and Complete Citation | Date | Abstract | Study Type | G.Tom +, N, - | P.Tom +, N, - | F.Tom +, N, - | Lyco +, N, - | Other +, N, - |
|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes | Olmedilla B | Reference values for retinol, tocopherol, and main carotenoids in serum of control and insulin-dependent diabetic Spanish subjects. Olmedilla B, Granado F, Gil-Martinez E, Blanco I, Rojas-Hidalgo E. Clin Chem. 1997 Jun;43(6 Pt 1):1066-71. | 1997 | To establish reference ranges for use in clinical and epidemiological studies, we determined concentrations of retinol, alpha-tocopherol, beta-carotene, alpha-carotene, beta-cryptoxanthin, lutein, zeaxanthin, and lycopene in 450 Spanish control subjects and 123 Spanish patients with insulin-dependent diabetes mellitus (IDDM). Results were grouped according to sex, and samples were collected throughout the year. Concentrations of retinol were significantly lower and beta-carotene and alpha-carotene were higher in women than in men, both in controls and IDDM subjects, whereas beta-cryptoxanthin concentrations were higher only in control women. Conditional logistic regression analysis showed that retinol, beta-carotene, and lycopene were the variables associated with diabetes. In comparison with other populations, our controls showed, in general, ordinary concentrations of retinol, comparatively low beta-carotene and high beta-cryptoxanthin concentrations, and a relatively high alpha-tocopherol/ cholesterol ratio. | CC | | | | (+) | |
| Diabetes | Rock CL | Racial group differences in plasma concentrations of antioxidant vitamins and carotenoids in hemodialysis patients. Rock CL, Jahnke MG, Gorenflo DW, Swartz RD, | 1997 | Approximately 50% of the mortality in hemodialysis patients is due to cardiovascular disease. Antioxidant vitamins and carotenoids may be protective because oxidation of low-density lipoproteins appears to be a necessary prerequisite for the development of atherogenesis, and hemodialysis itself may stimulate the generation of oxygen reactive species. African Americans comprise a substantial proportion of dialysis patients because they have higher rates of hypertension, glomerulonephritis, and diabetic end-stage renal disease than do whites. The purpose of this cross-sectional study was to | CS | | | | N | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Messana JM.<br><br>Am J Clin Nutr. 1997 Mar;65(3):844-50. | | determine the plasma concentrations of antioxidant vitamins and carotenoids in hemodialysis patients and to investigate whether differences in these concentrations in the major racial or ethnic groups exist. Plasma concentrations of alpha- and gamma-tocopherol, carotenoids, and retinol were measured with HPLC and plasma vitamin C was measured with a spectrophotometric method in 109 white and African American hemodialysis patients. Dietary intakes of selected micronutrients were also compared by using data from a food-frequency questionnaire. Overall, plasma vitamin C and alpha-tocopherol concentrations were comparable but plasma carotenoid concentrations were lower than those reported for other populations. African American patients had significantly higher mean plasma concentrations of retinol ($P < 0.04$), lutein ($P < 0.02$), and total carotenoids minus lycopene ($P < 0.04$); whites had significantly higher mean plasma concentrations of alpha-tocopherol ($P < 0.02$), independent of age and plasma lipid concentrations. Diabetes comorbidity had an independent negative association with plasma beta-carotene concentration but was not associated with other measures. | | | | | | |
| Diabetes | Chuang CZ | Risk factors for coronary artery disease and levels of lipoprotein(a) and fat-soluble antioxidant vitamins in Asian Indians of USA.<br><br>Chuang CZ, Subramaniam PN, LeGardeur BY, Lopez A.<br><br>Indian Heart J. 1998 May-Jun;50(3):285-91. | 1998 | High rates of coronary artery disease have been reported in the Asian Indians who have migrated to other countries. Although many coronary artery disease risk factors (diabetes, high serum cholesterol, lipoprotein[a], and smoking) have been suggested, studies of coronary artery disease risk factors in Asian Indians living in USA are only a few. We investigated coronary artery disease risk factors in 110 Asian Indian physicians living in USA by questionnaire and measurement of their serum lipids and fat-soluble antioxidant vitamins. Differences in risk factors between genders, vegetarian diets and diabetic status were also studied. We found that lipoprotein(a) (mean=20 mg/dl), low density lipoprotein cholesterol, and diabetes (prevalence of 7.5%) are more important risk factors for coronary artery disease, but not smoking, when compared to | CS | | | | (-) | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | other Americans. Higher levels of low density lipoprotein cholesterol, retinol, alpha-tocopherol, cryptoxanthin and lycopene, and lower levels of high density lipoprotein cholesterol were found in the males than in females. Comparable levels of lipoprotein(a) were found for males and females. Vegetarians, compared to non-vegetarians, had similar levels of lipids and fat-soluble antioxidants. Lower levels of retinol, lutein/zeaxanthin and lycopene were found in the diabetics compared to non-diabetics. These findings suggest that (1) the control of low density/high density lipoprotein cholesterol levels could be important in prevention of coronary artery disease in Indian males, (2) the vegetarian diets of Asian Indians do not favourably influence the serum lipid and antioxidant levels, and (3) increased serum levels of antioxidants may be beneficial for diabetics. Furthermore, for the first time, we show that serum levels of lutein/zeaxanthin and lycopene are significantly lower in the diabetics. | | | | | | |
| Diabetes | Granado F | Carotenoids, retinol and tocopherols in patients with insulin-dependent diabetes mellitus and their immediate relatives.<br><br>Granado F, Olmedilla B, Gil-Martínez E, Blanco I, Millan I, Rojas-Hidalgo E.<br><br>Clin Sci (Lond). 1998 Feb;94(2):189-95. | 1998 | 1. Patients with insulin-dependent diabetes mellitus are classified among the groups at risk for low vitamin status, and ecent studies suggest that some degree of supplementation with antioxidants may be beneficial in helping to prevent certain long-term complications of diabetes mellitus. Our objective was to compare the status of the fat-soluble vitamins and antioxidant-related compounds in patients with well-defined insulin-dependent diabetes mellitus with that of their irst-degree relatives, controlling seasonal and analytical variability as factors influencing the interpretation of the data.<br><br>2. Fifty-four patients with insulin-dependent diabetes mellitus, 214 non-diabetic, first-degree relatives (controls) and 236 unrelated controls were analysed for retinol, tocopherols (alpha and gamma) and main carotenoids in serum (beta-carotene, alpha-carotene, beta-cryptoxanthin, | CC | | | | N | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | lutein, zeaxanthin and lycopene) by means of a validated HPLC method.<br><br>3. Insulin-dependent diabetes mellitus was associated with lower retinol levels and higher levels of beta-carotene, alpha-carotene and beta-cryptoxanthin than sex-matched, first-degree relatives. alpha-Tocopherol, the alpha-tocopherol/cholesterol ratio, gamma-tocopherol, lutein, zeaxanthin and lycopene showed no differences. Retinol and beta-carotene were the variables most closely associated with diabetes<br><br>4. Patients with insulin-dependent diabetes mellitus showed lower serum retinol status together with higher concentrations of provitamin-A carotenoids. Serum fat-soluble antioxidant levels were greater than or equal to those in controls. According to the serum status observed, individuals with diabetes do not require supplementation with alpha-tocopherol or carotenoids, although the need for retinol supplementation in patients with marginal serum levels should be evaluated. | | | | | | |
| Diabetes | Ford ES | Diabetes mellitus and serum carotenoids: findings from the Third National Health and Nutrition Examination Survey.<br><br>Ford ES, Will JC, Bowman BA, Narayan KM.<br><br>Am J Epidemiol. 1999 Jan 15;149(2):168-76. | 1999 | Little is known about carotenoids, a diverse group of plant compounds with antioxidant activity, and their association with diabetes, a condition characterized by oxidative stress. Data from phase I of the Third National Health and Nutrition Examination Survey (1988-1991) were used to examine concentrations of alpha-carotene, beta-carotene, cryptoxanthin, lutein/zeaxanthin, and lycopene in 40- to 74-year-old persons with a normal glucose tolerance (n = 1,010), impaired glucose tolerance (n = 277), newly diagnosed diabetes (n = 148), and previously diagnosed diabetes (n = 230) based on World Health Organization criteria. After adjustment for age, sex, race, education, serum cotinine, serum cholesterol, body mass index, physical activity, alcohol consumption, vitamin use, and carotene and energy intake, geometric means of beta-carotene | CS | | | | (-) | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | were 0.363, 0.316, and 0.290 micromol/liter for persons with a normal glucose tolerance, impaired glucose tolerance, and newly diagnosed diabetes, respectively (p = 0.004 for linear trend), and geometric means for serum lycopene were 0.277,<br>0.259, and 0.231 micromol/liter, respectively (p = 0.044 for linear trend). All serum carotenoids were inversely related to fasting serum insulin after adjustment for confounders (p < 0.05 for each carotenoid). If confirmed, these data suggest new opportunities for research that include exploring a possible role for carotenoids in the pathogenesis of insulin resistance and diabetes. | | | | | | |
| Diabetes | Jang Y | Differences in body fat distribution and antioxidant status in Korean men with cardiovascular disease with or without diabetes.<br><br>Jang Y, Lee JH, Cho EY, Chung NS, Topham D, Balderston B.<br><br>Am J Clin Nutr. 2001 Jan;73(1):68-74. | 2001 | BACKGROUND: Abnormal body fat distribution and reduced antioxidant status have been shown to be effective markers of risk of cardiovascular disease (CVD).<br><br>OBJECTIVE: The objective of this study was to determine the differences in body fat distribution and antioxidant status in healthy men (control subjects) and in men with CVD with or without diabetes.<br><br>DESIGN: An oral-glucose-tolerance test was performed and CVD patients were subdivided into groups according to the presence or absence of diabetes. Adipose tissue areas were calculated from computed tomography scans made at the L1 and L4 vertebrae. Fasting serum concentrations of lipids, testosterone, insulin-like growth factor I, antioxidants, and plasma homocysteine were determined.<br><br>RESULTS: There were no significant differences in mean age, body mass index (in kg/m(2)), or blood pressure between the groups. The visceral fat area at the L1 vertebra was nonsignificantly greater in CVD patients without diabetes than in control subjects, whereas it was significantly greater in CVD patients with diabetes than in control subjects at both the L1 and L4 vertebrae. Both | CC | | | | (-)<br><br>Lowest in men with CVD and DM vs Controls or CVD alone | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | groups of CVD patients had higher plasma concentrations of homocysteine and lower serum insulin-like growth factor I concentrations and superoxide dismutase activities than did control subjects. Serum ss-carotene and lycopene concentrations were lowest in the CVD patients with diabetes.<br><br>CONCLUSION: The concurrent presence of CVD and diabetes is associated with a greater negative effect on the risk factors typically associated with significant declines in health status | | | | | | |
| Diabetes | Kanková K | Polymorphisms 1704G/T and 2184A/G in the RAGE gene are associated with antioxidant status.<br><br>Kanková K, Márová I, Záhejský J, Muzík J, Stejskalová A, Znojil V, Vácha<br><br>J. Metabolism. 2001 Oct;50(10):1152-60. | 2001 | The formation of advanced glycation end products (AGEs) and oxidative stress are supposed to play an important role in the development of diabetic late complications. AGEs can bind to several binding sites including receptor of advanced glycation end products (RAGE). AGE-RAGE interaction results in free radical generation. The aim of the present study was to investigate the impact of previously described polymorphisms in the RAGE gene (G82S, 1704G/T, 2184A/G, and 2245G/A) on the glycoxidation status in non-insulin-dependent diabetes mellitus (NIDDM). A total of 371 unrelated caucasian subjects were enrolled in the study. The NIDDM group consisted of 202 subjects, and the presence of late diabetic complications in 5 particular localizations was expressed as an index (I(compl)). The nondiabetic group included 169 subjects. Glycated hemoglobin (HbA(1c)), glycated stratum corneum proteins (Amadori, AGE), total carotenoids, alpha- and beta -carotene, gamma-tocopherol, lutein, lycopene, and alpha-tocopherol were measured in each subject. Statistically significant differences in allele frequencies between the NIDDM and the nondiabetic groups were observed for the G82S and 2245G/A polymorphisms (P =.047 and .032, respectively). HbA(1c), Amadori, and AGE did not reveal any significant association with any of the polymorphisms analyzed. However, significant differences between subjects bearing "wild-type majority" genotypes 1704GG+2184AA and subjects with "mutated" genotypes were found for | CC | | | | (-)<br>With RAGE gene polymorphisms for DM | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | total carotenoids (P =.001), alpha-carotene (P =.046), beta-carotene (P =.028), lutein (P =.001), lycopene (P =.006), and alpha-tocopherol (P =.047). I(compl) significantly correlated with the plasma levels of all antioxidants (all P <.01), while no correlation of I(compl) with glycation variables was observed. The newly identified intron polymorphisms in the RAGE gene were proved to be associated with the antioxidant status in NIDDM subjects. The extent of diabetic vascular disease is related to the plasma levels of antioxidants. | | | | | | |
| Diabetes | Ford ES | The metabolic syndrome and antioxidant concentrations: findings from the Third National Health and Nutrition Examination Survey.<br><br>Ford ES, Mokdad AH, Giles WH, Brown DW.<br><br>Diabetes. 2003 Sep;52(9):2346-52. | 2003 | Oxidative stress may play a role in the pathophysiology of diabetes and cardiovascular disease, but little is known about antioxidant status among individuals with the metabolic syndrome who are at high risk for developing these conditions. Using data from the Third National Health and Nutrition Examination Survey (1988-1994), we compared circulating concentrations of vitamins A, C, and E; retinyl esters; five carotenoids; and selenium in 8,808 U.S. adults aged > or = 20 years with and without the metabolic syndrome. After adjusting for age, sex, race or ethnicity, education, smoking status, cotinine concentration, physical activity, fruit and vegetable intake, and vitamin or mineral use, participants with the metabolic syndrome had significantly lower concentrations of retinyl esters, vitamin C, and carotenoids, except lycopene. With additional adjustment for serum lipid concentrations, vitamin E concentrations were significantly lower in participants with the metabolic syndrome than those without the syndrome. Retinol concentrations were similar between the two groups. After excluding participants with diabetes, the results were very similar. Consumption of fruits and vegetables was also lower among people with the metabolic syndrome. Adults with the metabolic syndrome have suboptimal concentrations of several antioxidants, which may partially explain their increased risk for diabetes and cardiovascular disease. | CS | | | | N<br><br>MetS vs non-MetS | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes | Bates CJ | Nutrient intakes; biochemical and risk indices associated with Type 2 diabetes and glycosylated haemoglobin, in the British National Diet and Nutrition Survey of people aged 65 years and over.<br><br>Bates CJ, Lean ME, Mansoor MA, Prentice A.<br><br>Diabet Med. 2004 Jul;21(7):677-84. | 2004 | AIMS: To characterize nutritional differences between survey participants diagnosed with Type 2 diabetes; those without diabetes, and those with "undiagnosed diabetes" based on glycosylated haemoglobin (HbA(1c)).<br><br>SUBJECTS AND METHODS: The 1994/5 British National Diet and Nutrition Survey, of people aged 65 years and over (mean age 78 years), included 73 respondents with diagnosed Type 2 diabetes [mean (sd) HbA(1c) = 7.06 (2.05)%], and 30 with "undiagnosed diabetes" (defined as HbA(1c) > 6.3%; mean (sd) HbA(1c) = 7.40 (1.66)%], among a representative sample of 1038 with anthropometry; 4-day weighed diet; blood and urine status measurements.<br><br>RESULTS: The prevalence of Type 2 diabetes (diagnosed + undiagnosed) was 10%. In subjects without diagnosis of diabetes, those with HbA(1c) > 6.3% had on average a significantly higher body weight (73.6 vs. 67.9 kg), higher waist circumference (99.8 vs. 91.8 cm), higher body mass index (28.6 vs. 25.9 kg/m(2)) and higher white cell counts (7.64 vs. 7.09 x 10(9)/l), than those with mean HbA(1c) < or = 6.3%. Diagnosed diabetic subjects had significantly higher energy-adjusted intakes of protein, fibre, vitamins and minerals than those not in this category (P < 0.01). In contrast, those with undiagnosed diabetes (HbA(1c) > 6.3%) were nutritionally "at risk", having low plasma concentrations of lycopene (0.13 vs. 0.24 micromol/l) and high density lipoprotein cholesterol (0.99 vs. 1.27 micromol/l) and a trend towards low vitamin C (24 vs. 36 micromol/l) which was significant (P < 0.01) for men. HbA(1c) was positively correlated with white cell count, plasma fasting triglycerides, plasma alkaline phosphatase and homocysteine (all P < 0.01 overall), being particularly striking amongst men.<br><br>CONCLUSIONS: Among older British citizens, those with diagnosed diabetes had healthier nutritional profiles than those undiagnosed with high | CS | | | | (-)<br><br>in undiagnosed | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | HbA(1c). Important health-promoting benefits are therefore predicted following early diagnosis and nutritional advice for people with Type 2 diabetes. | | | | | | |
| Diabetes | Coyne T | Diabetes mellitus and serum carotenoids: findings of a population-based study in Queensland, Australia.<br><br>Coyne T, Ibiebele TI, Baade PD, Dobson A, McClintock C, Dunn S, Leonard D, Shaw J.<br><br>Am J Clin Nutr. 2005 Sep;82(3):685-93. | 2005 | BACKGROUND: Epidemiologic evidence suggests that serum carotenoids are potent antioxidants and may play a protective role in the development of chronic diseases including cancers, cardiovascular disease, and inflammatory diseases. The role of these antioxidants in the pathogenesis of diabetes mellitus remains unclear.<br><br>OBJECTIVE: This study examined data from a cross-sectional survey to investigate the association between serum carotenoids and type 2 diabetes. DESIGN: Study participants were adults aged > or = 25 y (n = 1597) from 6 randomly selected cities and towns in Queensland, Australia. Study examinations conducted between October and December 2000 included fasting plasma glucose, an oral-glucose-tolerance test, and measurement of the serum concentrations of 5 carotenoid compounds.<br><br>RESULTS: Mean 2-h postload plasma glucose and fasting insulin concentrations decreased significantly with increasing quintiles of the 5 serum carotenoids--alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein/zeaxanthin, and lycopene. Geometric mean concentrations for all serum carotenoids decreased (all decreases were significant except that of lycopene) with declining glucose tolerance status. Beta-carotene had the greatest decrease, to geometric means of 0.59, 0.50, and 0.42 micromol/L in persons with normal glucose tolerance, impaired glucose metabolism, and type 2 diabetes, respectively (P < 0.01 for linear trend), after control for potential confounders.<br><br>CONCLUSIONS: Serum carotenoids are inversely associated with type 2 diabetes and impaired glucose metabolism. Randomized trials of diets | CS | | | | (-)/N<br><br>(-)<br><br>Fasting Insulin<br>2-hour Glucose<br><br>~~~~~<br>N<br><br>Total glucose<br>T2DM | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | high in carotenoid-rich vegetables and fruit are needed to confirm these results and those from other observational studies. Such evidence would have very important implications for the prevention of diabetes. | | | | | | |
| Diabetes | Hozawa A | Associations of serum carotenoid concentrations with the development of diabetes and with insulin concentration: interaction with smoking: the Coronary Artery Risk Development in Young Adults (CARDIA) Study.<br><br>Hozawa A, Jacobs DR Jr, Steffes MW, Gross MD, Steffen LM, Lee DH.<br><br>Am J Epidemiol. 2006 May 15;163(10):929-37. Epub 2006 Apr 5. | 2006 | Smoking is associated with low serum carotenoid concentrations. Prospective studies have found lower diabetes risk among persons with high-carotenoid diets. Whether diabetes risk is low in the rare smoker who has high serum carotenoid levels is unknown. The authors investigated the interaction of serum carotenoid concentrations and smoking with diabetes mellitus in 4,493 Black and White men and women aged 18-30 years in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. The authors assessed 15-year (1985-2001) incident diabetes (148 cases), insulin concentration, and insulin resistance (homeostasis model assessment) in smokers and nonsmokers according to baseline levels of serum alpha-carotene, beta-carotene, zeaxanthin, beta-cryptoxanthin, and lycopene. Diabetes incidence was inversely associated with the sum of carotenoid concentrations in nonsmokers (per standard deviation (SD) increase, relative hazard = 0.74, 95% confidence interval: 0.55, 0.99) but not in current smokers (relative hazard = 1.13, 95% confidence interval: 0.83, 1.53) (p for interaction = 0.02). Similarly, year 15 insulin and insulin resistance values, adjusted for baseline levels, were inversely related to sum of carotenoids only in nonsmokers (per SD increase in insulin level, slope = -0.46 (p = 0.03); per SD increase in insulin resistance, slope = -0.14 (p = 0.01)). In CARDIA, higher serum carotenoid concentrations are associated with lower risk of diabetes and insulin resistance in nonsmokers but not in smokers. | PC | | | | N<br><br>DM<br>IR | (-)<br><br>Total carotenoids |
| Diabetes | Sugiura M | The homeostasis model assessment-insulin resistance index is inversely associated with | 2006 | BACKGROUND: Carotenoids may reduce the risk for diabetes mellitus, but little is known about the association of<br>insulin resistance with serum carotenoids in non-diabetic subjects. This study aimed to investigate whether the | CS | | | | (-)<br><br>Women<br>~~~~~<br>N | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | serum carotenoids in non-diabetic subjects.<br><br>Sugiura M, Nakamura M, Ikoma Y, Yano M, Ogawa K, Matsumoto H, Kato M, Ohshima M, Nagao A.<br><br>J Epidemiol. 2006 Mar;16(2):71-8. | | homeostasis model assessment-insulin resistance (HOMA-IR) index would be lower in the presence of high serum carotenoid concentrations in non-diabetic subjects.<br><br>METHODS: A total of 812 subjects (256 males and 556 females) who had received health examinations in 2003 participated in the study. The associations of the serum-carotenoid concentrations and HOMA-IR were evaluated cross-sectionally. The multivariate-adjusted geometric means of HOMA-IR by the tertiles of the serum carotenoid concentration were calculated after adjusting for age, body mass index, systolic blood pressure, total cholesterol, triacylglycerols, current tobacco use, regular alcohol intake, exercise habits and total energy intake. Associations among high HOMA-IR (3.0+mUxmmol/L2) across tertiles of serum carotenoid concentration were assessed by tests for logistic regression analysis.<br><br>RESULTS: In male subjects, the multivariate adjusted geometric mean of HOMA-IR was inversely associated with the serum beta-cryptoxanthin concentrations. In female subjects, an inverse association of the serum carotenoid concentration and HOMA-IR was observed in lycopene, beta-cryptoxanthin, and zeaxanthin. The confounding factor-adjusted odds ratios (OR) for high HOMA-IR on the highest tertiles of serum alpha-carotene, beta-carotene, beta-cryptoxanthin, and zeaxanthin were 0.18 [95% confidence interval (CI): 0.06-0.52], 0.22 (95% CI: 0.07-0.67), 0.34 (95% CI: 0.12-0.96), and 0.30 (95% CI: 0.11-0.79), respectively, in male subjects. On the other hand, in female subjects, the adjusted OR for high HOMA-IR on the | | | | | Men<br><br>HOMA | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | highest tertiles of serum lycopene and beta-cryptoxanthin were 0.39 (95% CI: 0.21-0.73) and 0.51 (95% CI: 0.28-0.95), respectively.<br><br>CONCLUSIONS: The serum antioxidant carotenoids were inversely associated with HOMA-estimated insulin resistance in non-diabetic subjects. | | | | | | |
| Diabetes | Wang L | Plasma lycopene, other carotenoids, and the risk of type 2 diabetes in women.<br><br>Wang L, Liu S, Pradhan AD, Manson JE, Buring JE, Gaziano JM, Sesso HD.<br><br>Am J Epidemiol. 2006 Sep 15;164(6):576-85. Epub 2006 Jun 26. | 2006 | The authors conducted a nested case-control study from 1992 to 2003 among US women aged 45 years or older and free from cardiovascular disease and cancer to examine the prospective association among plasma lycopene, other carotenoids, and the risk of developing type 2 diabetes. During 10 years of follow-up, 470 cases of incident type 2 diabetes were selected and individually matched on age (+/- 1 year) and follow-up time to 470 nondiabetic controls. Baseline plasma levels of lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin were similar in cases and controls (all p > 0.05). A possible crude inverse association between plasma lycopene and risk of type 2 diabetes was attenuated upon multivariate adjustment. After control for plasma total cholesterol and known diabetes risk factors, the multivariate odds ratios of type 2 diabetes in the highest versus the lowest quartile of plasma carotenoids were 1.13 (95% confidence interval (CI): 0.60, 2.13) for lycopene, 1.27 (95% CI: 0.63, 2.57) for alpha-carotene, 1.10 (95% CI: 0.57, 2.13) for beta-carotene, 0.91 (95% CI: 0.46, 1.81) for beta-cryptoxanthin, and 1.35 (95% CI: 0.68, 2.69) for lutein/zeaxanthin. There was no prospective association between baseline plasma carotenoids and the risk of type 2 diabetes in middle-aged and older women. | CC nested | | | | N | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes | Wang L | Associations of plasma carotenoids with risk factors and biomarkers related to cardiovascular disease in middle-aged and older women.<br><br>Wang L, Gaziano JM, Norkus EP, Buring JE, Sesso HD.<br><br>Am J Clin Nutr. 2008 Sep;88(3):747-54. | 2008 | BACKGROUND: Cardiovascular disease (CVD) risk factors may potentially influence plasma concentrations of carotenoids. However, data on the association of plasma carotenoids with CVD related biomarkers are only limited.<br><br>OBJECTIVE: We examined the cross-sectional association of plasma carotenoids with blood lipids, glycated hemoglobin (Hb A(1c)), and C-reactive protein (CRP) in middle-aged and older women initially free of CVD and cancer.<br><br>DESIGN: Participants from 3 nested case-control studies in the Women's Health Study were pooled. Baseline plasma carotenoids, including alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, and lutein-zeaxanthin, blood lipids, Hb A(1c), and CRP were available for 2895 women. RESULTS: Women who were current smokers or obese had lower plasma concentrations of most carotenoids expect for lycopene. After adjusting for age, race, lifestyle factors, clinical factors, plasma total cholesterol, and dietary carotenoids, an increase of 30 mg/dL in LDL cholesterol was associated with a 17% increase in alpha-carotene, a 16% increase in beta-carotene, and an 8.5% increase in lycopene; an increase of 10 mg/dL in HDL cholesterol was associated with a 5.3% decrease in lycopene; an increase of 0.3% in Hb A(1c) was associated with a 1.4% increase in lycopene; and an increase of 2 mg/L in CRP was associated with a 1.3% decrease in beta-carotene (all $P < 0.01$).<br><br>CONCLUSIONS: In middle-aged and older women free of CVD and cancer, plasma carotenoids were associated with smoking, obesity, LDL cholesterol, HDL cholesterol, Hb A(1c), and CRP. The associations differ among individual carotenoids, possibly reflecting metabolic effects of lifestyle and physiologic factors on plasma carotenoids, and may partially explain the inverse association of plasma carotenoids with CVD outcomes observed in epidemiologic studies | CS | | | | (+) | HDL<br>Hb A(1c) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes | Brazionis L | Plasma carotenoids and diabetic retinopathy.<br><br>Brazionis L, Rowley K, Itsiopoulos C, O'Dea K.<br><br>Br J Nutr. 2009 Jan;101(2):270-7. Epub 2008 Jun 13. | 2009 | Diabetic retinopathy increases with duration of diabetes and may be associated with carotenoid status. Carotenoids alter the pro-oxidation/antioxidation balance, and circulating levels depend largely on dietary intake. Lower levels have been reported in diabetes and age-related macular degeneration; however, little is known of the relationship between carotenoids and diabetic complications. Consequently, the purpose of the present study was to evaluate the relationship between plasma carotenoids and diabetic retinopathy. We assessed the carotenoid-retinopathy relationship in 111 individuals with type 2 diabetes in a community-based, cross-sectional study. We photodocumented retinal status and used HPLC to measure plasma carotenoid concentrations. Data for clinical and demographic variables and risk factors for diabetic retinopathy were obtained from 24 h urine and fasting blood samples, and an interviewer-assisted lifestyle questionnaire. We found that the combined lycopene and lutein/zeaxanthin (non-pro-vitamin A (non-PVA) carotenoid) concentration when compared with the pro-vitamin A (PVA) carotenoids (alpha-carotene, beta-carotene and beta-cryptoxanthin) was significantly lower in the retinopathy than non-retinopathy group (OR 1.2 (95% CI 1.0, 1.4) v. 1.6 (95% CI 1.4, 1.7), respectively; P=0.009). A higher non-PVA:PVA ratio also predicted a lower risk of diabetic retinopathy, after adjustment for potential confounders (OR 0.33 (95% CI 0.12, 0.95); P=0.039). Finally, a higher concentration of PVA carotenoids was associated with greater odds of diabetic retinopathy, after adjustment for risk factors (P=0.049). We suggest synergies between carotenoids are implicated in diabetic retinopathy, independent of established risk factors. Importantly, our observations indicate dietary modulation of retinopathy risk may be possible by increasing intakes of lutein- and lycopene-rich foods. | CS | | | | (-) | Retin-opathy |
| Diabetes | Mutch DM | Metabolite profiling identifies candidate | 2009 | BACKGROUND: Roux-en-Y gastric bypass (RYGB) surgery is associated with weight loss, improved insulin sensitivity and glucose homeostasis, and a | Interv | | | | N | HOMA |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | markers reflecting the clinical adaptations associated with Roux-en-Y gastric bypass surgery.<br><br>Mutch DM, Fuhrmann JC, Rein D, Wiemer JC, Bouillot JL, Poitou C, Clément K.<br><br>PLoS One. 2009 Nov 19;4(11):e7905. | | reduction in co-morbidities such as diabetes and coronary heart disease. To generate further insight into the numerous metabolic adaptations associated with RYGB surgery, we profiled serum metabolites before and after gastric bypass surgery and integrated metabolite changes with clinical data.<br><br>METHODOLOGY AND PRINCIPAL FINDINGS: Serum metabolites were detected by gas and liquid chromatography-coupled mass spectrometry before, and 3 and 6 months after RYGB in morbidly obese female subjects (n = 14; BMI = 46.2+/-1.7). Subjects showed decreases in weight-related parameters and improvements in insulin sensitivity post surgery. The abundance of 48% (83 of 172) of the measured metabolites changed significantly within the first 3 months post RYGB ($p<0.05$), including sphingosines, unsaturated fatty acids, and branched chain amino acids. Dividing subjects into obese (n = 9) and obese/diabetic (n = 5) groups identified 8 metabolites that differed consistently at all time points and whose serum levels changed following RYGB: asparagine, lysophosphatidylcholine (C18:2), nervonic (C24:1) acid, p-Cresol sulfate, lactate, lycopene, glucose, and mannose. Changes in the aforementioned metabolites were integrated with clinical data for body mass index (BMI) and estimates for insulin resistance (HOMA-IR). Of these, nervonic acid was significantly and negatively correlated with HOMA-IR ($p = 0.001$, $R = -0.55$).<br><br>CONCLUSIONS: Global metabolite profiling in morbidly obese subjects after RYGB has provided new information regarding the considerable metabolic alterations associated with this surgical procedure. Integrating clinical measurements with metabolomics data is capable of identifying markers that reflect the metabolic adaptations following RYGB. | | | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes and lycopene | Polidori MC | Plasma levels of lipophilic antioxidants in very old patients with type 2 diabetes.<br><br>Polidori MC, Mecocci P, Stahl W, Parente B, Cecchetti R, Cherubini A, Cao P, Sies H, Senin U.<br><br>Diabetes Metab Res Rev. 2000 Jan-Feb;16(1):15-9. | 2000 | BACKGROUND: Experimental research indicates that oxidative stress is implicated in aging and in the pathogenesis of diabetes and its complications. This evidence is limited in elderly patients with non-insulin dependent diabetes, in which age- and disease-related production of reactive oxygen species might exert synergistic damaging effects on tissues and organs.<br><br>METHODS: Plasma levels of lipid-soluble compounds with antioxidant properties including vitamin A, vitamin E and carotenoids (lutein, zeaxanthin, beta-cryptoxanthin, lycopene, alpha- and beta-carotene) were measured by HPLC in 72 elderly patients with non-insulin dependent diabetes (75.7+/-0.8 years, 40 F, 32 M) and in 75 age-matched controls (77.2+/-1.2 years, 48 F, 27 M).<br><br>RESULTS: All compounds measured were significantly lower in plasma from diabetic patients as compared to controls ($p<0.0001$). Plasma levels of vitamins A and E and of carotenoids did not significantly correlate with dietary intake and lipid profile in both groups. In patients, significant inverse correlations were found between age and levels of vitamin E, beta-cryptoxanthin, lycopene and beta-carotene.<br><br>CONCLUSIONS: We conclude that patients of very old age with Type 2 diabetes show a poor plasma status of vitamins A and E and carotenoids, which negatively correlates with age. Further studies are needed to explore the possible therapeutic role of lipid-soluble vitamin supplements in elderly diabetic subjects. | CC | | | | (-)<br><br>DM vs Control | |
| Diabetes: oxidation | Bates JH | Antioxidant status and lipid peroxidation in diabetic pregnancy.<br><br>Bates JH, Young | 1997 | Pregnancy in insulin-dependent diabetes mellitus is associated with a greater incidence of fetal abnormality. Animal studies suggest that increased free-radical production and antioxidant depletion may contribute to this risk. The aim of the present study was, therefore, to assess nutritional antioxidant status and lipid peroxidation | CC | | | | N | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | IS, Galway L, Traub AI, Hadden DR.<br><br>Br J Nutr. 1997 Oct;78(4):523-32. | | in diabetic mothers in comparison with a control group. A 7 d dietary history and a food-frequency questionnaire were performed and venous blood collected for biochemical analyses from thirty-eight diabetic mothers and matched control subjects before 12 weeks gestation. Protein intake was significantly greater in diabetic patients (81.4 (SE 14.8) v. 72.7 (SE 15.8) g/d, P = 0.015), while total sugar intake was less (79.5 (SE 13.2) v. 104.8 (SE 28.8) g/d, P < 0.001). There were no significant differences in the intake of the major antioxidant vitamins (retinol, vitamin C or vitamin E) or beta-carotene. However, intakes of a number of other micronutrients (including Se, Zn, Mg, Mn, riboflavin, thiamin, niacin and folate) were greater in diabetic patients. Among the nutritional chain-breaking antioxidants, serum levels of alpha-tocopherol (21.6 (SE 5.7) v. 17.3 (SE 4.7) mumol/, P = 0.0013), beta-carotene (0.27 (SE 0.18) v. 0.14 (SE 0.11) mumol/l, P = 0.003) and lycopene (0.23 (SE 0.17) v. 0.16 (SE 0.13) mumol/l, P = 0.03) were greater in diabetic patients. There was no evidence of greater lipid peroxidation in diabetic patients, and total antioxidant capacity was similar in the two groups. Overall, these results indicate that nutritional antioxidant status is better in this group of diabetic mothers than in control pregnant non-diabetic subjects attending the same maternity hospital. | | | | | | |
| Diabetes: MetS | Beydoun MA | Serum antioxidant status is associated with metabolic syndrome among U.S. adults in recent national surveys. Beydoun MA, Shroff MR, Chen X, Beydoun HA, Wang Y, Zonderman AB.<br><br>J Nutr. 2011 May;141(5):903- | 2011 | Potential antiinflammatory and antioxidant effects were recently ascribed to naturally occurring micronutrients. The<br>extent and magnitudes of their differential effects on the metabolic syndrome (MetS) are still unknown. We examined<br>the association between serum antioxidant status and MetS. NHANES 2001-2006 cross-sectional data among adults aged 20-85 y were analyzed (n = 3008-9099). MetS was defined with the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and also by elevated homeostatic model assessment insulin resistance (HOMA-IR), C-reactive protein (CRP) and hyperuricemia. Serum antioxidants included retinol, retinyl esters, carotenoids [α-carotene, β- | CS | | | | (-)<br>MetS<br><br>in a CC analysis<br><br>N<br>MetS<br>CS OR analysis | HOMA<br>CRP<br><br>N |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 13. Epub 2011 Mar 30. | | carotene (cis+trans), β-cryptoxanthin, lutein+zeaxanthin, total lycopene], vitamin E, and vitamin C. MetS (NCEP ATP III) prevalence in U.S. adults was 32.0% among men and 29.5% among women. Adults with MetS had consistently lower serum carotenoid concentrations compared with those without MetS, even after controlling for total cholesterol and TG among other potential confounders. Vitamin E had no significant relationship with MetS in the full multiple logistic regression model, whereas retinol+retinyl esters were inversely related to MetS among men only. The latter were also inversely related to elevated CRP and positively associated with hyperuricemia. Vitamin C exhibited a similar pattern to serum carotenoids with an inverse linear association with MetS (binary), HOMA-IR, and hyperuricemia. Future intervention studies of dietary and lifestyle change must be conducted to assess the utility of modifying serum antioxidant concentrations, especially carotenoids, given their suboptimal levels among U.S. adults with MetS, for the prevention of type 2 diabetes and various cardiovascular endpoints. | | | | | | |
| Diabetes: T2DM | Li ZZ | Serum lycopene levels in patients with diabetic retinopathy.<br><br>Li ZZ, Lu XZ, Ma CC, Chen L.<br><br>Eur J Ophthalmol. 2010 Jul-Aug;20(4):719-23. | 2010 | PURPOSE: Accumulating evidence indicates that oxidative stress may play an important role in the pathogenesis of type 2 diabetes and its complications. Lycopene, a very potent antioxidant of carotenoids, has received considerable scientific interest in recent years for its potential role in the prevention of oxidative stress-related chronic diseases. This study was undertaken to investigate whether the serum levels of lycopene are altered between type 2 diabetic patients with and without diabetic retinopathy.<br><br>METHODS: A total of 71 patients with type 2 diabetes were analyzed and compared with 23 nondiabetic healthy controls. Serum lycopene concentrations were assayed using high-performance liquid chromatography. | CC | | | | (-)<br><br>↓ PL in T2DM vs Control<br><br>~~~~~<br>(-)<br>HbA1c | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | RESULTS: Lycopene level was found to be significantly lower in diabetic patients than in controls (p = 0.021). In the diabetic group, subjects with proliferative diabetic retinopathy had significantly lower lycopene levels than subjects without diabetic retinopathy or with nonproliferative diabetic retinopathy. In the analysis of correlations, hemoglobin A1c were negatively correlated with lycopene (r = -0.345, p = 0.007) after multivariate adjustment. A stepwise linear multiple regression model revealed that age and hemoglobin A1c were significant determinants of lycopene.<br><br>CONCLUSIONS: Our findings show that measuring serum lycopene is a novel convenient method for evaluating oxidative damage. Diabetic patients, especially those with advanced diabetic retinopathy, had significantly lower serum lycopene levels; this suggests that lycopene may be helpful for the diagnosis, severity, and therapeutic evaluation of diabetic retinopathy. | | | | | | |
| Diabetes: TIDM | Azar M | Serum carotenoids and fat-soluble vitamins in women with type 1 diabetes and preeclampsia: a longitudinal study.<br><br>Azar M, Basu A, Jenkins AJ, Nankervis AJ, Hanssen KF, Scholz H, Henriksen T, Garg SK, Hammad SM, Scardo JA, Aston CE, Lyons TJ.<br><br>Diabetes Care. 2011 | 2011 | OBJECTIVE: Increased oxidative stress and immune dysfunction are implicated in preeclampsia (PE) and may contribute to the two- to fourfold increase in PE prevalence among women with type 1 diabetes. Prospective measures of fat-soluble vitamins in diabetic pregnancy are therefore of interest.<br><br>RESEARCH DESIGN AND METHODS: Maternal serum carotenoids (α- and β-carotene, lycopene, and lutein) and vitamins A, D, and E (α- and γ-tocopherols) were measured at first (12.2 ± 1.9 weeks [mean ± SD], visit 1), second (21.6 ± 1.5 weeks, visit 2), and third (31.5 ± 1.7 weeks, visit 3) trimesters of pregnancy in 23 women with type 1 diabetes who subsequently developed PE (DM PE+) and 24 women with type 1 diabetes, matched for age, diabetes duration, HbA(1c), and parity, who did not develop PE (DM PE-). Data were analyzed without and with adjustment for | CS | | | | N | Pregnancy<br><br>PE |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Jun;34(6):1258-64. Epub 2011 Apr 15. | | baseline differences in BMI, HDL cholesterol, and prandial status.<br><br>RESULTS: In unadjusted analysis, in DM PE+ versus DM PE-, α-carotene and β-carotene were 45 and 53% lower, respectively, at visit 3 ($P < 0.05$), before PE onset. In adjusted analyses, the difference in β-carotene at visit 3 remained significant. Most participants were vitamin D deficient (<20 ng/mL), and vitamin D levels were lower in DM PE+ versus DM PE- throughout the pregnancy, although this did not reach statistical significance.<br><br>CONCLUSIONS: In pregnant women with type 1 diabetes, low serum α- and β-carotene were associated with subsequent development of PE, and vitamin D deficiency may also be implicated. | | | | | | |