

989-39 Antioxidant Supplementation Reduces the Susceptibility of Low Density Lipoprotein (LDL) to Oxidation in Patients With Coronary Artery Disease

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We studied the effect of a combination of vitamin E, vitamin C, and beta-carotene on the susceptibility of LDL to oxidation, as determined by lag phase (minutes), in a 12 week clinical trial of 45 patients with coronary artery disease (CAD), mean age 60.6 ± 8.6 years. Subjects were randomized to one of the following interventions (15 each): 1) placebo; 2) vitamin E 400 IU, vitamin C 500 mg, beta-carotene 12 mg (mid dose); or 3) vitamin E 800 IU, vitamin C 1000 mg, beta-carotene 24 mg (high dose). Two baseline, one 6 week and two 12 week measurements of standard lipoproteins and lag phase (Lag) were obtained. Compared to baseline, 12 week plasma concentrations of alpha-tocopherol increased 2 and 3 fold; vitamin C increased 1.5 and 2 fold; and beta-carotene increased 6 and 10 fold in the mid and high dose groups respectively with no change in the placebo group. Lag significantly increased from baseline (190.1 ± 63.8) to 12 weeks (391.1 ± 153.0) in the high dose group ($p < 0.01$). No significant within group change for Lag was observed for the placebo or mid dose group at 12 weeks. A significant between group difference in Lag was observed at 12 weeks, attributable to high dose vs. placebo ($p < 0.05$). Results were not altered by adjusting for age, sex or other significant clinical predictors of lag phase. We conclude supplementation with a combination of antioxidant vitamins reduces the susceptibility of LDL to oxidation in patients with CAD. These results may be significant for the secondary prevention of CAD.

989-40 Cholesterol Lowering Reduces the Incidence of and May Improve Event-Free Survival After Coronary Revascularization

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To assess the impact of effective cholesterol lowering on the subsequent need for coronary revascularization (CRVASC) and event-free survival following CRVASC in hypercholesterolemic survivors of a single myocardial infarction (MI), the results of cholesterol lowering by partial ileal bypass (PIB) in the Program on the Surgical Control of the Hyperlipidemias (POSCH) trial and the POSCH Long-Term Follow-Up Study were reviewed. During POSCH (1975–1990), total cholesterol was 23.3% lower, LDL cholesterol was 37.7% lower, and HDL cholesterol was 4.3% higher in the PIB-treated intervention group ($n = 421$) versus the diet-treated control group ($n = 417$). With long-term follow-up complete until September 30, 1994 (mean follow-up = 13.8 ± 2.0 years), 186 control and 98 intervention group patients underwent CRVASC by either PTCA or CABG ($p < 0.0001$ by Mantel-Haenszel test; relative risk = 0.42 (95% CI: 0.33–0.54) for CRVASC in the intervention group). The decision to perform CRVASC was made by referring physicians acting independently of POSCH. Analysis of post-CRVASC events (mean follow-up = 7.3 ± 3.9 years) demonstrated:

Post-CRVASC Event	Control	PIB	p	RR (95% CI)
Overall mortality	31	12	0.3	0.71(0.50–1.88)
ACHD mortality	21	9	0.6	0.79(0.36–1.73)
ACHD mortality or non-fatal MI	81	34	0.1	0.72(0.48–1.07)
N	186	98		

p values by Cox regression. ACHD = atherosclerotic coronary heart disease. RR = relative risk in intervention group.

Effective cholesterol lowering by PIB in POSCH reduced the subsequent need for CRVASC by 47% with follow-up extending to nearly 14 years. Trends toward improved event-free survival after CRVASC were evident in the cholesterol lowered group.

989-41 Seasonal Variation in Ischemic Heart Disease Mortality: The Relative Effects of Temperature, Sunlight, and Respiratory Infection

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To study the relative effects of temperature, direct sunlight, and respiratory disease on the seasonal variation in ischemic heart disease (IHD) mortality, we examined 10-year data (1984–1993) from Hawaii. We used linear regression to test for seasonal differences in IHD mortality rates and multiple linear regression to assess the effects of average monthly temperature, percent of direct sunlight, and pneumonia or influenza mortality rates.

The average IHD mortality rate was significantly lower during summer (Jun–Aug) compared with winter (Dec–Feb) (11 deaths/100,000 vs 14 deaths/100,000, $p = 0.03$). Multiple regression analysis revealed that average monthly temperature ($p = 0.01$) and bacterial or viral pneumonia mortality rates ($p < 0.001$) were significantly associated with the IHD mortality rate, whereas the average monthly percent of direct sunlight was not. These 3 variables together explained over 99% of the seasonal variation in IHD mortality. An increase in pneumonia mortality of 1 death/100,000 population was associated with an increase in IHD mortality of 2 deaths/100,000 population (95% CI 1.5–2.5). A 1-degree decrease in temperature was associated with an increase in IHD mortality of 0.13 deaths/100,000 population (95% CI 0.04–0.21).

We conclude that temperature and respiratory infections are both independently associated with IHD mortality, and their seasonal variation may explain winter-summer fluctuations in IHD mortality rates.

989-42 Birthweight Is Related to Endothelial Function in Systemic Arteries of Young Children (Aged Eight to Eleven Years)

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Epidemiological evidence has suggested an inverse correlation between birthweight (BW) and subsequent risk from ischemic heart disease, but the underlying basis has not been studied. As endothelial dysfunction is an early event in atherogenesis, we used high resolution ultrasound to examine endothelium-dependent dilation in the brachial arteries of 321 children aged 8 to 11 years to examine the relationship to BW and conventional risk factors including cholesterol, blood pressure and smoking history (active and passive). Vessel diameter was measured at rest and after reactive hyperemia, induced by cuff occlusion and release on the forearm, and scans were analysed by two independent observers. Reproducibility was excellent when tested in 30 children (correlation between scans, $r = 0.8$, $p < 0.001$). Flow mediated dilation (FMD) was not related to age, sex, body mass index, cotinine, cholesterol, blood pressure or degree of reactive hyperemia. There was, however, a significant correlation with vessel size ($r = -0.34$, $p < 0.001$) and BW ($r = 0.16$, $p = 0.003$) with FMD being lowest in children with lower birthweights. This suggests that endothelial function, an important factor in atherogenesis, is related to birthweight in normal children independent of conventional risk factors. This is consistent with the proposal that factors in utero may programme risk for later cardiovascular disease.

989-43 State Death Certificates Can Be Used to Identify Cases of Sudden Cardiac Death

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We used the MITI Registry linked to the Medic-One paramedic database and State of Washington death certificates to develop a novel method for identifying patients with sudden cardiac death (SCD). From an original cohort of 32,239 patients admitted to Seattle-area hospitals between 1988 and 1993, 901 patients were treated for possible out of hospital cardiac arrest after discharge from initial hospitalization. Based on cardiac rhythm and symptoms at the time of presentation, the patients were divided into cardiac arrest versus non-cardiac arrest.

State death certificate records were then used to classify this same group of patient deaths as either sudden or non-sudden based on place of death and ICD-9 codes. Patients who died at home of either a neoplasm or trauma/suicide as well as all hospital deaths were classified as non-sudden; all other deaths were classified as sudden.

The application of this death certificate-based classification system resulted in 89% accurate identification of SCD.

We conclude that death certificate data when modified by ICD-9 coding can be used to reasonably identify sudden cardiac death in a cohort of patients with known or suspected coronary disease.

989-44 The Effect of a Water Intake on the Morning Surge of Platelet Activity

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Acute cardiovascular events occur in a prominent circadian pattern with a morning increase in frequency. To investigate whether a water intake before retiring to bed could prevent the morning increase of platelet activities, hemostatic and platelet functions were evaluated in 21 hospitalized patients with various coronary risk factors. Blood samples were collected 4 times in each patient. "Sample 1" was drawn 30 minutes after supper. The patients