**ABSTRACTS - Vascular Disease, Hypertension, and Prevention**

### Platelet-Activating Factor-Like Lipids Mediate Endothelial Cell Apoptosis Induced by Hypercholesterolemic Low-Density Lipoprotein

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**Background:** Atherosclerosis is an inflammatory disease and platelet-activating factor (PAF)-like lipids are potent proinflammatory factors. However, their role in the apoptosis of endothelial and smooth muscle cells (SMC) has not been identified. We recently demonstrated that LDL, the most electron-dense and a mildly oxidized subfraction of LDL isolated from hypercholesterolemic human plasma, induces apoptosis in cultured UC. Methods: We tested the mediator role of PAF-like lipids in LDL-induced apoptosis. As a reference, the effects of LDL were compared with those of well-characterized copper-oxidized LDL (oxLDL). Results: In bovine aortic EC cultures, both LDL (50 µg/mL) and oxLDL (50 µg/mL) inhibited fibroblast growth factor 2 (FGF2) transcription and Akt phosphorylation. Concomitantly monitored Bcl-2 family proteins revealed reduced expression of Bcl-2 and increased expression of Bax. FGF2 overexpression preserved Akt phosphorylation and prevented the Bcl-2-dependent apoptosis. WEB-2086 is an antagonist for the Gi-coupled PAF receptor (PAFR) or PAF-like receptors. WEB-2086 (10 µM) or a Gi-deactivator pertussis toxin (100 nM) effectively attenuated FGF2 downregulation and the associated apoptosis in cells exposed to either LDL or oxLDL. Phospholipids isolated from oxLDL also induced apoptosis by downregulating FGF2. Pretreating LDL and oxLDL-derived phospholipids with a recombinant PAF-acylethanolamide, a phospholipase A2 that specifically hydrolyzes the short-chain acyl group in phospholipids, abolished their effects. In conclusion, treating LDL and oxLDL-derived phospholipids with phospholipase A2 had no influence on their effects. Conclusion: Our findings indicate that PAF-like mediates the apoptotic signal of LDL circulating in patients with hypercholesterolemia. OxLDL mimics LDL functionally because its signal is mediated by similar mediators.

### The Modification of Epitopes on Low Density Lipoprotein by Homocysteine May Affect the Affinity of LDL to LDL Receptors

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**Background:** ApoB-100 is the only lipoprotein component in low density lipoprotein (LDL). The intravascular metabolism of apoB-100 remains unclear. The increase of LDL in plasma and hyperhomocysteinemia are the important cardiovascular risk factors. Theaflavins are formed when green tea is fermented to produce black tea. Animal studies show that green tea catechins and black tea polyphenols increase fecal excretion of fat and cholesterol. Hypothesis: A green tea extract enriched with theaflavins will have a favorable effect on the lipid profile of subjects with mild to moderate hypercholesterolemia. Methods: A double-blind, randomized, placebo-controlled, parallel-group trial involving 240 men and women age 18 years or older on a low fat diet with baseline LDL between 130-190 mg/dl in 6 outpatient clinics in China. Subjects were given a daily capsule containing theaflavin-enriched green tea extract (370 mg) or placebo for 12 weeks. Results: Mean levels (±SEM) of total cholesterol, LDL, high density lipoprotein cholesterol (HDL), and triglycerides changed by -11.3 ± 0.9 (P=0.01), -11.6 ± 1.1 (P=0.01), 2.5 ± 2.1 (P=NS), and 6.9 ± 5.5 (P=NS) respectively in the tea extract group. Mean levels of total cholesterol, LDL, HDL, and triglycerides did not change significantly in the placebo group. No significant adverse events were observed. Conclusions: Theaflavin-enriched green tea extract is an effective adjunct to a low fat diet to lower LDL in hypercholesterolemic adults and is well tolerated.

### Mediterranean and Low Fat Diets Are Associated With Similar Lipid Levels at 12 Months In Patients With Coronary Heart Disease on Statin Therapy

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**Background:** A low fat diet is recommended for patients with coronary heart disease (CHD). A high fat Mediterranean diet, rich in monounsaturates (MUFAs) is associated with low CHD rates and is as effective as Low Fat in lowering cholesterol. Long-term relative efficacy of diets for patients on statins is unknown. This study compared Low Fat to Mediterranean diets on lipids and lipoproteins in patients on CHU on standard therapy (including statins). Methods: 89 patients with angiographic CHD were randomised to Low Fat (fat 20-25 % of Energy, saturated fat 8-10 % energy) or Mediterranean (fat 36-40 % energy, > 50% of fat as MUFA). Lipids were measured prior to drug therapy, at randomisation and at 3 and 12 months. Results: At randomisation and 12 months, 86 % Low Fat patients and 83 % Mediterranean patients were on statins. Similarly, 80% Low Fat and 85% Mediterranean patients were taking aspirin. Mean fat intake in Low Fat diet was 20% of total energy (SFA 8.5 % of total energy) compared to Mediterranean diet with fat 34% of total energy (57 % of fat as MUFA). Conclusions: Mediterranean and Low Fat diets are associated with similar lipid and lipoprotein levels at one year in patients with CHD on standard therapy. Recommendations for CHD patients ought to consider a Mediterranean diet as an alternative to Low Fat.

### Effects of a Carbohydrate-Restricted Diet Versus a Fat- and Calorie-Restricted Diet on Lipid Subfractions

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**Introduction:** Low carbohydrate (Low Carb) diets have recently gained popularity. While preliminary data suggest no adverse effect of a Low Carb diet on standard serum lipid levels, there is concern that such diets may adversely shift lipid subfractions to a more atherogenic profile relative to a fat- and calorie-restricted (Low Fat) diet. We randomized 80 subjects with severe obesity and a high prevalence (79%) of diabetes in metabolic syndrome to a Low Carb versus a Low Fat diet, and assessed the effects on lipid subfractions known to increase risk of coronary artery disease (CAD) (small dense low density lipoprotein (LDL) cholesterol particles and large very low density lipoprotein (VLDL) particles), as well as effects on large high density lipoprotein (HDL) cholesterol particles which have been shown to be protective against CAD. Methods: After randomization, subjects received intensive instruction on a Low Carb versus a Low Fat diet. Lipid particle sizes were measured using nuclear magnetic resonance spectroscopy at 0 months, from which concentrations (expressed in median (interquartile range)) of lipid subfractions were derived. Results: Low Carb group subjects experienced a greater decrease in large VLDL (from 46.15 ± 10.0 mg/dl to 21.38 ± 9.6 mg/dl (p=0.031). The Low Carb group demonstrated a trend toward a greater decrease in small dense LDL particle concentration (from 0.533 ± 0.8 mg/dl (p=0.08) versus the Low Fat group (from 0.630 ± 0.8 mg/dl (p=0.13). Subjects in the Low Carb group also demonstrated a trend toward a greater increase in the concentration of large HDL particles in the Low Carb group (increasing from 12.7 ± 16.8 mg/dl to 14.11 (2.23) mg/dl versus the Low Fat group (from 10.7 (6.16) mg/dl (p=0.05). Conclusions: Subjects with severe obesity and a high prevalence of diabetes or metabolic syndrome demonstrate a shift to a more favorable lipid subfraction profile after 6 months on a carbohydrate-restricted diet compared to a calorie- and fat-restricted diet.