

## ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #069

### 1. Title:

Dietary and Endogenous Anti-Oxidants and Atherosclerosis  
Data Analysis Proposal to the ARIC Publications Committee

### 2. Proposed Group Members:

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### 3. Background:

As recently reviewed by Steinberg et al. (1989), the oxidation of lipids in LDL may be an important step in the development of atherosclerosis. Four events which are thought to play a role in atherosclerosis plaque formation have been observed after the oxidation of LDL; (1) increased chemotaxis of circulating monocytes, (2) inhibition of macrophage migration, (3) enhanced uptake of LDL by macrophages through the acetyl-LDL receptor leading to foam cell generation, and (4) frank cytotoxicity, facilitating endothelial denudation. Moreover, Stringer et al. (1989) report elevated plasma lipid peroxide concentrations in patients with either coronary heart disease or peripheral artery disease compared to controls.

There is evidence that LDL peroxide formation is preventable. Szczeklik et al. (1985) found that Vitamin E supplementation reduce plasma lipid peroxide concentration in humans. In restricted ovulator hens, Vitamin E supplementation reduced the rate of intimal thickening in hen aortas (Smith and Kummerow, 1989). The role of other anti-oxidants in the prevention of either LDL oxidation or atherosclerosis has been largely unexplored. But, beta-carotene has been shown to increase LDL's resistance to  $\text{Cu}^{++}$  oxidative modifications (Quintao et al., 1989). and Crouse et al. (1987) found uric acid concentrations to be inversely correlated with B-mode ultrasound scores of the carotid arteries.

### 4. Aim:

Examine the role of endogenous and dietary anti-oxidants in atherosclerosis. The potential implication of a (negative) association between dietary anti-oxidants and atherosclerosis applies to the question of the modification of dietary intake to influence atherosclerotic risk.

### 5. Hypothesis:

Dietary and endogenous anti-oxidants are inversely associated with atherosclerotic lesion development. The analysis will examine the relations between atherosclerosis and (1) individual anti-oxidants (from Frei, 1988): Vitamin C (dietary), Vitamin E (dietary), total carotenoids (dietary), beta-carotene (dietary), uric acid (blood), and bilirubin (blood); (2) water soluble anti-oxidants (Vitamin C and Uric Acid), (3) lipid soluble anti-oxidants (Vitamin E, total carotenoids, and bilirubin), and (4) total anti-oxidants. A score will be developed for analysis categories 2-4.

### 6. Data Needed:

Dietary: Vitamin C, Vitamin E, total carotenoids, beta-carotene, total calories.

Laboratory: Uric acid, bilirubin, albumin, LDL-C, HDL-C (Vitamin E, Vitamin C and beta-carotene, if available).

Medical Examination: Systolic blood pressure, diastolic blood pressure, height, weight

Other baseline data: Smoking history, age, race, sex.

Outcomes data: B-mode, prevalent CVD events.

### References:

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Quintao E, Witztum JL, Parthasarathy S, Elam R, Steinberg D (1989). Role of beta-carotene in the oxidative modification of low density lipoproteins. *Circulation* 80:II-380.

Smith TL, Kummerow FA (1989). Effect of dietary vitamin E on plasma lipids and atherogenesis in restricted ovulator chickens. *Atherosclerosis* 75:105-109.

Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL (1989). Beyond cholesterol: modifications of low-density lipoprotein that increase its atherogenicity. *N Engl J Med* 320:915-924.

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Szczeklik A, Gryglewski RJ, Domagala B, Dworski R, Basista M (1985). Dietary supplementation with vitamin E in hyperlipoproteinemias: effects on plasma lipid peroxides, antioxidant activity, prostacyclin generation and platelet aggregability. *Thrombosis and Haemostasis* 54:425-430.